

# South African Medical Journal

## Suid-Afrikaanse Tydskrif vir Geneeskunde

P.O. Box 643, Cape Town

Posbus 643, Kaapstad

Cape Town, 24 December 1955  
Weekly 2s. 6d.

Vol. 29 No. 52

Kaapstad, 24 Desember 1955  
Weekliks 2s. 6d.

### VAN DIE REDAKSIE

#### INTERKAPILLÈRE SKLEROSE VAN DIE NIERLIGGAAMPIES

Hierdie kondisie is in 1936 vir die eerste maal deur Kimmelstiel en Wilson<sup>1</sup> beskryf op grond van hulle waarnemings van letsels tussen die haarvate in die nierliggaampies. Dit is 'n ontaarding van diabetes mellitus en is algemeen bekend as die siekte van Kimmelstiel en Wilson, diabetiese sklerose van die nierliggaampies, of diabetiese niersiekte. Die oorsaak van hierdie kondisie is onbekend, maar die huidige mening is dat dit saamhang met die algemene bloedvatkomplikasies van diabetes en dat dit veroorsaak word deur die biochemiese veranderinge teweeggebring deur suikersiekte. Mukopolysakkariede is al in die bloed en bloedvate van pasiënte met interkapillère nierliggaamsklerose aangetoon, maar dit is nog nie definitief vasgestel of hulle wel 'n oorsaaksfaktor van hierdie siekte is nie. Soms word 'n hoë gehalte lipoproteïene aangetoon, maar soms verskyn dit eers nadat die niersiekte reeds ontwikkeld het.

Volgens nadoodse studies van die niere van diabetiese pasiënte wissel die voorkomssyfer van interkapillère sklerose van die nierliggaampies tussen 19.5 en 30 persent in verskillende reekse.<sup>2</sup> Dit kom meer dikwels onder ouer pasiënte voor by wie suikersiekte al 'n paar jaar lank teenwoordig was voordat die nierkomplikasie ontmasker is—maar in 'n sekere reeks<sup>3</sup> was die meeste gevallen jong mense. Onder jong pasiënte is mans en vrouens ewe vatbaar vir hierdie komplikasie van suikersiekte.

Die siekte kom voor by pasiënte wat diabetes in ligtegraad gehad het sowel as by persone by wie dit ernstig was. Faktore soos die duur van die suikersiekte, en die mate van beheer daaroor, is van belang by die patogenese van nierliggaamsklerose. Maar dit is moeilik om die duur van die suikersiekte vas te stel, veral by ouer pasiënte, aangesien die siekte jare lank voor uitkennings al teenwoordig kon wees. Dit word gemeen dat goeie suikersiektebeheer die nierkomplikasie vertraag en die strafheid daarvan verminder, maar verdere waarnemings hieroor is nodig om die stelling te staaf.

Interkapillère nierliggaamsklerose kan klinies uitgeken word aan die volgende verskynsels: drukverhoging,

### EDITORIAL

#### INTERCAPILLARY GLOMERULOSCLEROSIS

This condition was first described in 1936 by Kimmelstiel and Wilson<sup>1</sup> from their observations on the intercapillary lesions in the glomeruli of the kidney. It is a degenerative complication of diabetes mellitus and has come to be known as Kimmelstiel-Wilson's disease, diabetic glomerulosclerosis or diabetic kidney disease. The cause of the condition is unknown, but the disease is regarded at present as part of the generalized vascular complications of diabetes brought about by the biochemical changes of diabetes. Mucopolysaccharides have been demonstrated in the blood and the blood vessels of patients with intercapillary glomerulosclerosis, but whether they are a causal factor in the disease remains to be more firmly established. High lipoprotein values are sometimes obtained, but may not appear until after the renal disease has developed.

As judged by post-mortem studies of the kidneys of diabetic patients the incidence of intercapillary glomerulosclerosis varies from 19.5 to 30% in different series.<sup>2</sup> It occurs more frequently in older patients, diabetes having been present for several years before the renal complication manifests itself, but in one series<sup>3</sup> there was a majority of young patients. In young patients this complication of diabetes occurs approximately equally in both sexes.

The condition may occur both in patients who have had mild diabetes and in those in whom the diabetic condition is more severe. Such factors as the duration of diabetes and the degree of control of the disease are important factors in the pathogenesis of the glomerulosclerosis. But the duration of diabetes, especially in the older groups, is not easily established, since the disease may have been present for years before diagnosis was made. Good control of diabetes is believed to delay and minimize the severity of the renal complication, but further observations on this point are actually necessary.

edeem, diabetiese netvliesaandoenings, nierversaking, albuminurie en hipoalbuminurie.<sup>2</sup> Diagnose kan slegs gestaaf word deur nierbiopsie-studies of deur nadoodse ondersoek. In vroeë gevalle is drukverhoging nie noodwendig teenwoordig nie, of dit kan effe begin en dan in die loop van die siekte vererger. Dit is moeilik veral by ouer pasiënte, om te bepaal of die drukverhoging deur suikersiekte veroorsaak is; selfstandige drukverhoging, kroniese nierliggaamontsteking, die Cushing-syndroom en geswel van die niermurg se chromaffienweefsel moet almal in ag geneem word. Gewoonlik lever kliniese studies genoeg feite op om hierdie kondisies te onderskei, maar in sommige uitgesoekte gevalle kan naaldbiopsie gedoen word met betreklike veiligheid vir die pasiënt. Dit is egter nie 'n prosedure wat as roetine toegepas moet word nie.

Baie jare gelede is die netvliesaandoenings wat met suikersiekte gepaard gaan in 4 grade geklassifiseer.<sup>4</sup> Graad I en II word beskou as diabetes-soortlik, maar die verskynsels eie aan graad III en IV behoort gewoonlik by diabetes wat met drukverhoging gepaard gaan. Diabetiese netvliesveranderings verskyn gewoonlik voordat kliniese simptome van interkapillêre nierliggaamsklerose waarneembaar is.<sup>2</sup> Sommige mense meen dat dit die hewige grade van netvliesaandoenings is wat eintlik met nierliggaamsklerose in verband gebring moet word, maar soms kom hulle sonder enige kliniese tekens van nieraantasting voor.<sup>2</sup>

Dit is moeilik om die voorkomssyfer van edeem wat regstreeks deur hierdie siekte veroorsaak word te bepaal; hartversaking en ander oorsake van edeem kan teenwoordig wees. Fraksiebepalings van serumproteiene is belangrik al is daar geen edeem nie; hipoalbuminemie en omskakeling van die albumien-globulienverhouding sal aangetoon word, terwyl hipoalbuminemie dikwels voorkom voordat daar enige betekenisvolle veranderinge is in die totale serum-inhoud aan proteiene. By 'n diabetiese pasiënt kan albuminurie 'n vroeë teken wees van interkapillêre sklerose van die nierliggaampies, en mag die urine klein hoeveelhede globulien bevat. Uremie en bloedarmoede is tekens wat by die meeste pasiënte gevind word.

Soms het behandeling van diabetiese niersiekte tesame met behoorlike suikersiektebeheer gunstige gevolge.<sup>2</sup> Nierbehandeling kan verskillende maatreëls insluit soos ekstra proteen in die dieet as daar hipoalbuminemie sonder uremie is; inkorting van die natrium-inname by edeem, en moontlik die gebruik kan kwik-diureтика as die bloedureum onder 50 mg. per 100 ml. is. Bloed-oortappings kan waardevol wees by gevalle van ernstige bloedarmoede. Matige middels wat drukverhoging teewerk kan ook gebruik word.

1. Kimmelstiel, P. en Wilson, C. (1936): Amer. J. Path., **12**, 83.
2. Clark, A. M. en Skillern, P. G. (1955): Med. Clin. N. Amer., **39**, 1001.
3. Wilson, J. L., Root, H. F. en Marble, A. (1951): New Engl. Med. J., **245**, 513.
4. Wagener, H. D., Dry, T. J. en Wilder, R. M. (1934): *Ibid.*, **211**, 1131.

The features by which intercapillary glomerulosclerosis may be diagnosed clinically are hypertension, oedema, diabetic retinopathy, renal failure, albuminuria and hypoalbuminaemia.<sup>2</sup> Proof of the condition can only be obtained from renal biopsy studies or at post-mortem examination. In early cases hypertension may not be present, or it may be mild and become more severe as the disease progresses. The differentiation from hypertension due to other causes presents a problem, especially in older subjects; essential hypertension, chronic glomerulonephritis, chronic pyelonephritis, Cushing's syndrome and phaeochromocytoma may have to be considered. Clinical studies may be sufficient in most cases for differentiation of these conditions, but in some selected cases needle biopsy of the kidney may be done with relatively small risk to the patient; this, however, is not a procedure for routine use.

The retinitis (retinopathy) occurring in diabetes was classified many years ago<sup>4</sup> into 4 grades. While grades I and II are regarded as specific for diabetes, the features observed in grades III and IV usually occur in diabetes associated with hypertensive changes. Diabetic retinal changes usually precede the onset of the clinical symptoms of intercapillary glomerulosclerosis. The severe grades of retinopathy are said to be more likely to be associated with intercapillary glomerulosclerosis, but they may be present with no clinical evidence of renal involvement.<sup>2</sup>

The incidence of oedema directly due to this disease is difficult to determine accurately; cardiac failure and other causes of oedema may be present. Even in the absence of oedema, fractional determinations of serum protein are important; hypoalbuminaemia, and reversal of the albumin-globulin ratio will be demonstrated, while frequently hypoalbuminaemia occurs before significant changes in the total serum-protein level. Albuminuria in a diabetic patient may be an early sign of the presence of intercapillary glomerulosclerosis; small amounts of globulin are also present in the urine. Uraemia and anaemia are other features that will be found in the majority of patients.

Treatment of diabetic kidney disease, with proper control of the diabetes, may sometimes yield favourable results.<sup>2</sup> The renal treatment may include extra protein in the diet if there is hypoalbuminaemia without uremia, restriction of sodium intake if there is oedema, and possibly the use of mercurial diuretics if the blood urea is below 50 mg. per 100 ml. Blood transfusions may be of value for severe anaemia. Mildly-acting anti-hypertensive drugs may be considered.

1. Kimmelstiel, P. and Wilson, C. (1936): Amer. J. Path., **12**, 83.
2. Clark, A. M. and Skillern, P. G. (1955): Med. Clin. N. Amer., **39**, 1001.
3. Wilson, J. L., Root, H. F. and Marble, A. (1951): New Engl. Med. J., **245**, 513.
4. Wagener, H. P., Dry, T. J. and Wilder, R. M. (1934): *Ibid.*, **211**, 1131.

## THE ROLE OF RADIOTHERAPY IN THE TREATMENT OF MALIGNANT DISEASE\*

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A more accurate title for this paper would perhaps be 'The Role of Radiotherapy as a Curative Agent', because that is the element which I want to stress. Radiotherapy is still a young specialty. It is in one sense just over 50 years old, if we go back to the discoveries of radium and of X-rays. It is much younger than that if we go back only to its really effective beginnings. Any new specialty or, indeed, any new branch of medical practice, tends to evolve in much the same way. First there is the discovery itself, made in one particular aspect of medicine, or some new knowledge or a new machine is applied to a single disease. This, however, is almost at once followed by over-enthusiastic application to a wide, supposedly related field. One good example was the way that, after their discovery, the vitamins, although they have each a very defined special function, were applied to all sorts of conditions—and still are! The first harvest of this enthusiasm is an abundant outpouring of ill-founded and quite unscientific claims for the new agent, or new machine. This, in turn, often leads to a pendulum-swing in the opposite direction, to a sense of frustration and, for a period, to a denigration of the new medium. In the end, however, everything settles down and gradually the real scope and, equally important, the real limitations of the new medium become clear. Then gradually we see built up a solid structure of balanced knowledge, which constitutes a genuine addition to the armamentarium of medical science. So the specialty becomes, in part, stabilized.

I believe that radiotherapy as now practised in the United Kingdom, having been through each one of these stages, has very largely reached the stage of inherent stability. So we can outline, in part at least, where it fits into the whole pattern of medicine. In particular, I think we can define with some accuracy the part it ought to play in the treatment of malignant disease in any well-organized medical community. Later I will have some British figures to show you which bear on this point.

The primary purpose of this paper is, therefore, to try and set out in an orderly fashion the contributions which modern radiotherapy, in its fully developed form, can make to the control of malignant disease.

The first point to note is that radiation is employed in two quite distinct ways which, although they overlap, can be reviewed as separate entities. They are (1) its use as a primarily *palliative agent*, and (2) its deliberate employment as a *curative agent* for some types of cancer.

*Palliation*

Nowadays we have got so used to the application of radiation, particularly X-rays, for those temporary

beneficial effects which go by the name of palliation, that we almost forget that this phenomenon represents something quite new in the management of malignant disease. A few surgical measures such as colostomy and tracheotomy are solely palliative in purpose. With these exceptions, however, surgery in cancer, when it fails in its primary intention to cure, scarcely benefits the patient at all, although it may, for a short time, conceal under a nice clean flap the outward manifestations of disease.

In contrast, radiation, because of its capacity to induce growth restraint in all living tissue, can inhibit growth for substantial periods. In this way it can relieve pain, can clean up distressing ulceration, and can prolong and improve the quality of remaining life. This palliation has, too, a great psychological value in that once a patient has experienced distinct betterment, he can no longer be without some hope. He has seen for himself that something can be done. This effect is demonstrated most strikingly in lung cancer. Here radiotherapy can as yet offer little contribution to cure. Pneumonectomy, though valuable when applicable, is only applicable to a small minority of cases. Yet lung cancer has assumed the proportions of an epidemic disease, and presents a major challenge. It is our experience that some three-quarters of these patients with pain, cough, haemoptysis and even symptoms of considerable upper mediastinal compression, can be restored once, for a worth-while period, to something approaching the normal. As a result, right to the end, they can hang on to the idea that what has once been done for them might be done again and, almost to the last moment, they don't lose hope.

*Curative Functions*

At one time the palliative use of radiotherapy was perhaps its major contribution, and it still, indeed, remains a valuable by-product where we fail to cure. Its very usefulness, however, has perhaps blinded many to what is now the greater contribution of radiotherapy to the control of malignant disease, its real curative value in some types of neoplasia.

In certain cancers, radiation, properly applied, can be depended on to yield a rate of permanent cure of the order of 30-50% of all cases. When, however, we look only at the earlier cases of these cancer types, cure rates are genuinely high and fully justify my use of the term 'curative'. Be it noted, however, that such dividends can only be earned by a high quality of technique—and of radiotherapeutic organization. Cancer surgery today ties its successes to systematic and thought-out operations linked with high-quality supporting services, both in theatre and ward. So, too, radiotherapy might as well not be used if it is merely employed in a casual or haphazard way—'Give this patient a little X-ray please'. Nowadays it is to be looked on as a specialty in which possession of real experience and real knowledge is the

\* A paper presented in a symposium on the Treatment of Carcinoma held in plenary session at the South African Medical Congress, Pretoria, October 1955.

only condition under which it can be competently practised.

I would place this serious incursion of radiotherapy into the curative field as a development of the last 20 years. The contributions can in a broad way be grouped under 3 main heads:

1. A few types of malignant diseases previously incurable can now be brought under control.

2. It can be used as an adjunct to surgery.

3. It provides an alternative to surgery, either because of higher cure-rates, or because of superior functional results.

Let us look at each of these briefly.

#### *Malignant Diseases previously uncontrolled*

This group is best illustrated by a number of growths known to radiotherapists as the radio-sensitive tumours. Dr. Edith Paterson\* has analysed the situation in regard to these tumours as they affect children. Quite a number of growths fall into this peculiarly radio-sensitive category, some common, some rare. They mainly consist of the true sarcomas of the lympho-reticular system and the so-called embryonal carcinomas. The main examples of the group are lymphosarcoma, reticulosarcoma, lympho-epithelioma of the nasopharynx, a few thyroid tumours, Wilms' tumour of the kidney, medulloblastoma, seminoma testis, and dysgerminoma (ovary).

It is a curiously varied group but it has two common characteristics: (1) this high radio-sensitivity, and (2) marked tendency towards dissemination. The high radio-sensitivity has two consequences. One is that such tumours are very easy to cure if they happen to be small. The other and more important is that the dose which is sufficient for effective therapy can be given to large volumes of the body. This is fortunate as it in part cancels out the other character of this whole group—the depressing tendency to spread with extreme rapidity from the primary focus of origin, first locally and then systemically. In fact, the key to successful curative treatment becomes the irradiation in continuity of impressively large volumes of tissue. The sensitivity of this group has been known for a long time, but most of the older treatment-techniques have been conservative in regard to the volume treated. As a result all that was usually obtained was a spectacular but temporary palliation.

I am deliberately excluding from discussion here the lympho-reticular growths of an apparently systemic nature, such as Hodgkin's disease and the leukaemias. We can do much for these in a palliative way; I might indeed have taken them as another good example of palliative therapy. But they are not yet curable, and I want at the moment to keep real curability as my immediate text.

It is impossible here to discuss each of these tumours separately, but perhaps tables I and II illustrative of the results currently achieved at the Christie Hospital, Manchester, will help to focus the situation appropriately.

\*Paterson, E. (1955): *S. Afr. Med. J.* **29**, 1199 (17 December).

TABLE I. RADIO-SENSITIVE TUMOURS: 5-YEAR RESULTS OF ALL CASES TREATED 1934-48

Extent of Disease	Number Treated	5-year Survival
<i>Tumours of Nasopharynx:</i>		
Limited to N.P. .. .. ..	15	60%
With cervical nodes .. .. ..	50	42%
Generalized .. .. ..	11	0%
	76	40%
<i>Seminoma of Testis:</i>		
No demonstrable metastases ..	99	77%
Abdominal or pulmonary metastases ..	112	28%
	211	51%
<i>Medulloblastoma</i> .. .. ..		
	27	44%

TABLE II. WILMS' TUMOUR OF THE KIDNEY: 5-YEAR RESULTS OF 26 CASES TREATED 1940-49

Technique	Number Treated	5-year Survival
Radical: Nephrectomy followed by X-ray Therapy .. .. ..	10	50%
Radical: X-ray Therapy followed by Nephrectomy .. .. ..	9	33%
	19	42%
Palliative: X-ray Therapy .. .. ..	7	0%
	26	31%

#### *Radiotherapy as Adjunct to Surgery*

Here we can find no better illustration than breast cancer. Time was when every breast cancer which could be said to be technically operable was worth operating on. The results in the late cases were poor, and death in those which failed may even have been hastened; but there was no alternative and, clearly, some salvage was better than certain failure. Nowadays all over the world there has been a severe tightening up of the limits beyond which surgery is to be regarded as inadvisable, even though radical operation for the right cases remains the treatment of choice. Why this change? It is because radiotherapy in its own right can cure some cases, even in a semi-advanced stage, and thus take over that responsibility from surgery and add to it an immense palliative contribution. Not only so but, by the judicious joint application with surgery, the cure rates, even of the surgical cases, can be enhanced. This is true whether one believes in radical surgery in its proper place, or in the modified surgical approach advocated by Edinburgh. You will surmise from the way in which I phrased that sentence, that the latter is a restricted approach in which I do not believe.

#### *Radiotherapy Curative in its own Right*

Lastly, we come to a more controversial problem—the field where radiotherapy is becoming more and more accepted as a preferable alternative to surgery. I realize full well that here I begin treading on some toes and impacting on honestly held, but perhaps a little prejudiced opinion. All I can plead is that I will tread as gently as possible, but that also, in the end, reality has to be faced and accepted, for lives are at stake. There are 4 main

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cancers in which this is becoming increasingly true—those of the skin, the mouth and lip, the cervix uteri and, more recently, the bladder.

I am not going to inflict a lecture on each of these on you. The skin story, for example, is not one of survival—both good surgery and good radiotherapy are equally curative, but in some regions, especially the face and hands, the superior cosmetic results of radiotherapy cannot be denied. The cervix story I shall have the privilege of telling in one of the sectional meetings, of this Congress\*, and must not touch on here. I would like, however, to examine the two other cancers in greater detail as good examples of the general principle, namely mouth cancer and bladder cancer.

#### MOUTH CANCER

Perhaps the best illustration is mouth cancer, and the best way of telling it is through my own experience over the last 25 years. When I went to Manchester first, the standard treatment of mouth cancer was either operation or so-called radical diathermy but, because of the work of Regaud in Paris, the radium therapist was being given many of the late cases 'to see what he could do'. It quickly became apparent—and my predecessor in Manchester, Dr. Birkett, had already demonstrated it to a large B.M.A. Meeting—that radiotherapy could do quite a lot. Very soon, though not without some argument here and there, more and more earlier cases were referred and curability rose rapidly. In due course the new method became universally accepted in Manchester as superior to and better than surgery. So now I can say, without hesitation and with no fear that, were they here, I should be contradicted by any of my surgical colleagues, that radiotherapy is accepted as the primary treatment of intra-oral cancer. So much is this the case that mouth cancer tends more and more to be channelled through the radiotherapy clinics and wards, and to disappear from the general surgical clinics. This has obvious repercussions on teaching, for it is also true of some other radiotherapeutic cancers. The correct answer is patently obvious, namely that the radiotherapy clinics must take their due share of clinical teaching, like otolaryngology, gynaecology or other specialist groups who have over the years detached isolated segments of medicine from the general pool.

Let us look for a few moments at the detail of radiotherapeutic methods as applied to mouth cancer. Radium and X-rays, if properly used, are both effective. The mouth is one of the sites in which a high dose to a limited volume, which is the key to success in these epithelial tumours, is often best achieved by radium. It is my belief that even in many radiotherapeutic circles there is a tendency to overlook the distinct advantages which intra-oral radium methods have over any external radiation approach, except for lesions of the oro-pharynx and base of tongue. It is certainly superior to intra-oral X-ray. How radium will compete with megavoltage X-rays remains to be seen.

Mouth cancer is also a good first theme in that it

exemplifies most elegantly the infinite variety of techniques which may be employed and how technique has to be adapted intelligently to the particular localization of the growth.

*At this point a number of slides were shown illustrating the versatility of the different methods of treatment employed in mouth cancer.*

Tables III, IV and V give a picture of the mouth-cancer situation as assessed statistically: Table III shows the over-all 5 year survival for the last available group, contrasting early and late cases. Table IV analyses the results if we look at radical treatment only, omitting the hopelessly advanced stage-IV group. Table V shows over the last 20 years how improving technique has yielded a steadily improving percentage of cure.

TABLE III. TREATMENT OF MOUTH CANCER 1945-49: 5-YEAR NET SURVIVAL: EARLY-LATE RESULTS

Treatment	Stages I and II (555 cases)		Stages III and IV (486 cases)	
Radium	..	..	46%	16%
X-ray	..	..	32%	5%
Total	..	..	44%	9%

TABLE IV. RADICAL TREATMENT OF MOUTH CANCER: RESULTS OF CASES 1943-49

Treatment	Number of Cases	5-year Net Survival	
		Radical	Radical X-ray Small Field
Radium	..	..	870
Radical X-ray Small Field	..	..	200
Total Radical	..	..	1,070

TABLE V. RADICAL TREATMENT OF MOUTH CANCER: PROGRESSIVE RESULTS

Years	Number Treated	5-year Net Survival
1928-30	..	24%
1934-36	..	29%
1940-42	..	37%
1946-48	..	40%

Just as surgery succeeds only by meticulously detailed and well planned technique, so radiotherapy, to compete, must also be meticulous. In addition, to ensure success real clinical experience of the disease has to be linked with technical knowledge and adequate technical facilities. But when the 'know-how' is there, the method, as the tables show, cures cancer in percentages which no surgical series has ever approached.

#### CANCER OF THE BLADDER

The treatment of bladder cancer provides another useful, and I think interesting, illustration of my general thesis. In England treatment policy in bladder cancer is at present rapidly changing as the very real contributions of radiotherapy are being recognized, even although it is still in many places not yet the routine method of treatment.

What is the surgical background? The 3 main recognized treatments of bladder cancer are (1) cystoscopic

\* See Page 1228 of this issue.

fulguration, (2) partial cystectomy or open diathermy, and (3) total cystectomy. Each of these yields a fraction of cures, but any objective study makes it evident that the numbers cured are not high.

*Cystoscopic fulguration*, excellent though it is in the control of benign papillomata, is by its very nature inadequate for cancer. It contravenes every surgical principle that a radical approach is obligatory in the treatment of malignant disease anywhere.

*Partial cystectomy* could control growths of the fundus quite well, but it is obviously weak when applied in the bladder base and, unfortunately, that is where most growths appear.

*Cystectomy*, as a widely applied operation, depending as it does on modern antibiotics and other modern surgical aids, is of relatively recent origin. It certainly does obey the tenets of true radical surgery in that the operation is both wide and apparently complete. Yet even total cystectomy has real weakness towards the base. It is, moreover, a major undertaking both for surgeon and patient, and can only hold its place if there is nothing simpler of equal value. In the post-war decade it has been very instructive to watch, both in my own and other centres, the waning enthusiasm for this method as a primary treatment as soon as the value of radiotherapy became recognized in those centres in which it was competently practised.

In contrast, what has radiotherapy to offer? Again 3 methods are available: (1) Radon or radium implant at cystotomy, (2) radical X-ray therapy, and (3) Intravesical 'balloon'. Each has its proper place.

*Implant* is applied to the limited and defined lesion which formerly would have been dealt with by partial cystectomy, and is a task calling for collaboration between the radiotherapeutic and the genito-urinary departments.

*X-ray therapy* is for the later case and offers exceptional scope for what is now known as megavolt therapy—that is, radiation in the million-volt ranges. Ordinary radical X-ray therapy at conventional deep-therapy levels remains, however, entirely practical and such megavoltage is not essential.

*The bladder balloon* is of more recent evolution, but fills a much-needed niche for the extensive but superficial type of growth, either the mossy carcinoma or the multiple-papilloma type which has gone malignant. It either uses a radio-active cobalt slug as a central source or a radio-active fluid fills the balloon.

Once again it should be emphasized that radiotherapy represents a fully-matured technical approach, and that it is quality of technique and matured judgment in choice of technique which yields results.

*At this point slides were shown illustrating various methods of treatment employed.*

Two statistical tables are reproduced in Tables VI and VII. Table VI shows the rapid increase in the number of patients with cancer of the bladder who are referred for radiological treatment, as the possibilities of radiotherapy have gradually become better appreciated. Table VII shows the actual results of radical treatment by radon implant and by X-ray. It should be pointed out that the X-ray is reserved for the later

cases and this is not a comparison between gold seed and X-ray.

TABLE VI. CANCER OF THE BLADDER: NUMBER OF CASES SEEN AT CHRISTIE HOSPITAL

1934-37	..	..	..	100
1938-41	..	..	..	153
1942-45	..	..	..	228
1946-49	..	..	..	431
1950-53	..	..	..	714
1934-53	..	..	..	1,626

TABLE VII. RADICAL TREATMENT OF BLADDER CANCER: RESULTS OF CASES 1945-49

Treatment	Number of Cases	5-year Net Survival
Intravesical Implant (Seeds)	143	54%
Radical X-ray	74	30%
Total Radical	217	44%

#### DISCUSSION

The two cancers we have examined are, to my mind, good prototypes of what curative radiotherapy can do today for the more accessible squamous cancers. They are not by any means the only cancers of which this can be said. Indeed, I only present them to you as illustrative examples in a field which is still expanding. What is true of these two is also true to a large extent of a number of the carcinomas.

Let us now consider whether there are any useful generalizations which can be made over the whole field.

The first concerns radiotherapy alone and is the point I stressed earlier, that where cure is the aim with these epithelial tumours of limited sensitivity the key to success is high dosage to small volume, and that we are working at the limits of normal tissue-tolerance. This is true whether the treatment is by radium, by X-ray, or by a combination of the two. To get reliable results we are forced to provide not only a fairly high degree of specialized skill, but to back it when necessary with elaborate equipment and experienced lay staff, including the physicist.

The other point concerns the proper relationship between surgery and this modern radiotherapy. In the old experimental days of radiotherapy the radiologist was handed the late cases or post-operative recurrences, while surgery was given first choice, and rightly so. It was indeed a gloriously useful dumping ground! There are now certain fields in which the competent radiotherapist can offer radical curative treatment which is either simpler or better than surgery. In these fields radiotherapy should now come first if the maximum number of lives are to be saved. Surgery, however, remains available and continues to have a real contribution to make. My thesis is that the surgeon in these restricted fields must now accept it as being in the patient's best interest that he provides the second line of defence. Total *glossectomy* may save life where radium fails, and where it is the sole remaining radical approach. So, too, *cystectomy* may save the case which recurs after X-radiation—a recurrence particularly easy to diagnose.

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The number of cases, however, in which the full price of radical surgery is paid becomes in this way a much smaller fraction of all cases occurring and the maximum possible summation of results is achieved.

This concept of surgery as the treatment of second choice is one which the surgeon, very naturally, finds it emotionally hard to accept, until he has seen for himself the superior results of good radiotherapy.

#### Conclusion

In conclusion I want to look at this whole problem from quite a different angle. My aim is to put before you objective evidence that I have not been airing the pipe dreams of a radiotherapist on the way things ought to be organized in a Utopia. The evidence I have in mind is embodied in the next four slides.

In the first place let us examine the balance between radiotherapy and surgery. If we take all types of malignant disease together, including stomach and the other surgical cancers, and compare the number of cases treated surgically and the numbers treated by radiotherapy, what do we find? Table VIII shows the answer for the United Kingdom, using test groups of hospitals.

TABLE VIII. THE RATIO BETWEEN THE NUMBER OF CANCER CASES TREATED IN 1953 (a) BY RADIOTHERAPY AND (b) BY SURGERY (combined cases included in each column)

	% Total Treated Cases	
	Therapy	Surgery
<i>Provincial Hospitals</i>		
A Regional Survey	..	58
A University Hospital	..	55
A General Hospital	..	72
<i>London Hospital</i>		
A University Hospital (1949)	..	87
<i>Scottish Hospitals</i>		
A Regional Survey (1949)	..	67
A University Hospital	..	69

As you will see, radiotherapy is consistently called on to a greater extent. I think the ratio throughout is one

which many people would not have expected, and yet these represent British practice in its leading medical centres.

The other evidence comes from examination of the growth, over the last 15 years, of radiotherapy in its own right. If a method is useful and its results real, its application expands. If it is but a passing fashion it dies. Table IX is an up-to-date version of some figures

TABLE IX. GROWTH IN DEMAND FOR RADIOTHERAPY: PATIENTS WITH MALIGNANT DISEASE SENT TO RADIOTHERAPY CENTRES FOR TREATMENT

	1938	1953/54
<i>Provincial Hospitals:</i>		
'Cancer'	..	1,965
University Hospitals:		4,421
Region A	..	577
Region B	..	820
Region C	..	630
General	..	414
		1,554
		1,801
		2,574
		1,001
<i>London Hospitals:</i>		
'Cancer'	..	801
University	..	738
		1,624
		2,000
<i>Scottish Hospital:</i>		
University	..	654
		999

I got out for the Radiological Congress in 1950 to show how, despite the war, the use of radiotherapy had grown in Great Britain. I am now able to give in contrast the numbers of patients with malignant disease referred for radiotherapy in the year 1938 and the year 1953/54 in various English and Scottish centres.

The growth between 1938 and 1954 is impressive.

These are our British figures. They are, I believe, objective evidence that a worth-while contribution can be made by this new agent. It is, too, one which will be augmented still further by the application of isotopes and of megavoltage.

## CHEMOTHERAPY OF MALIGNANT DISEASE\*

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Christie Hospital and Holt Radium Institute, Manchester, England

The interest in a chemical approach to the treatment of malignant disease is a very old one, as old or older than surgery. For example, Avicenna in the 10th century recommended arsenic as an internal remedy for cancer and, much earlier, about 1,500 B.C., an ointment composed of arsenic and vinegar was used for external 'cancer'. These empiric potions, and many less elegant ones, have persisted through the ages and, however discredited, they still form the stock-in-trade of the present-day quack.

Modern chemotherapy of cancer, in contrast to the old empiricism, is of recent origin. It is based on experi-

mental work and on such hypotheses as seem reasonable and can be tested. Further, the growth of organic chemistry has extended the ability to synthesize compounds which, on theoretical grounds, might prove to be more potent. This is particularly well seen in the evolution of the group of compounds that stemmed from the study of the biological effects of mustard gas during the last war. Nevertheless, the workers in chemotherapy would be well advised to remain modest. The chemotherapeutic approach to cancer is not yet a curative one in any field. Palliation is so far the best that can be hoped for. It follows that chemotherapy should not be used in malignant disease if there is any hope of cure by either surgery or radiotherapy.

\* A paper presented at the South African Medical Congress, Pretoria, October 1955.

Because of the extent of the field of chemotherapy, I will exclude for this brief survey the contributions made by hormones, important though they are. My main emphasis will be placed on the following groups of substances: (1) The radiomimetic substances, being the mustard-like compounds and Myleran, (2) urethane, and (3) the large class of compounds known as antimetabolites. The examples I shall choose will be those with some claim to being of practical clinical value.

#### RADIOMIMETIC COMPOUNDS

In the group which are rather loosely labelled as 'radiomimetic', there are those stemming from the nitrogen mustards either because of similarity of formula or of chemical function. The nitrogen mustards are probably the most familiar (Fig. 1). HN2 was found to be quickly

#### NITROGEN MUSTARD

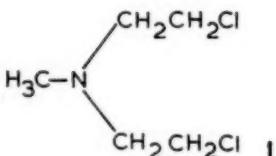


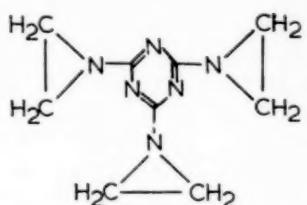
Fig. 1.

decomposed in the body into reactive transformation-products which become fixed to the cells. It was, therefore, a logical next step to synthesize compounds which already carried the same reactive groupings in their molecule. One of these is TEM, another TEPA and a third thioTEPA (Fig. 2).

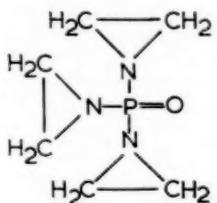
Fig. 2 shows the ethylenimino groups which are active. It has been stressed by Hendry *et al.* (1951) that at least two such groups should be present to obtain an inhibiting effect on tumours. All these compounds inhibit tumours in animals. In tumour tissue *in vitro*, HN2 inhibits glycolysis possibly by damaging the enzymes concerned with nucleic-acid metabolism. A decrease in viscosity of nucleic acids occurs with stickiness of chromosomes, similar to that produced by X-rays. Chromosome breaks are produced and if *Drosophila* flies are exposed to these substances, it has been shown that mutations occur in the offspring. There is every reason to expect, therefore, a profound influence on malignant disease but it will be obvious that normal cells, particularly cells in active division, will also be profoundly disturbed by chemicals so potent.

These compounds have a place mainly in the treatment of Hodgkin's disease, of lymphatic leukaemia, of polycythaemia vera and sometimes of other malignant reticuloses such as giant follicular lymphoma and generalized lymphosarcoma. The chemical effects of all those substances in this group are very similar. HN2 must be given intravenously and there is a risk of venous thrombosis. Patients are very often sick and nauseated for a few hours. As a compensation for this rather rough

#### TEM



#### TEPA



#### THIOTEPA

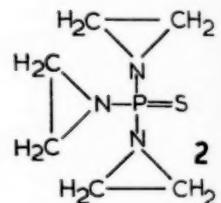


Fig. 2.

passage, the patient with systemic symptoms of Hodgkin's disease improves very rapidly following this treatment.

Triethylene melamine has the advantage that it can be given orally as enteric-coated tablets, and it produces less nausea. TEPA and thioTEPA are usually given intravenously; there is very little sickness and very little local reaction. These two newer compounds, triethylene phosphoramide and triethylene thiophosphoramide do not seem, meantime, to have any real clinical superiority over HN2 or TEM and they have the same dangers.

One of the most important clinical applications of the nitrogen mustards and their kindred forms is in the management of the generalized case of *Hodgkin's disease*. I feel that so long as the disease is localized, local irradiation with X-rays is the treatment of choice. Even when disease is generalized, irradiation is of great value in resolving isolated masses. However, when generalization occurs with systemic symptoms chemotherapy is preferable. It must be remembered that the chemotherapeutic approach is a systemic one. It is very important to avoid an excessive depression of bone marrow. Repetition of a course should only be done if the neutrophil and platelet counts are reasonably high. With this warning, I may add that I have given up to 9 courses of treatment to a patient in the course of 2 years with benefit each time.

Some years ago, we started a clinical experiment to find whether local X-radiation combined with nitrogen mustard had a more lasting beneficial effect on the patient. Cases were chosen in which only a single group of nodes were clinically invaded. The idea was that the HN2 would deal with small foci elsewhere in the body and if this occurred the survival of the patient might be

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TABLE I. HODGKIN'S DISEASE. LOCALIZED: RESULTS AT 3 YEARS

	Number Treated	Crude % Survival
Treated by HN2+X-ray	35	69%
Treated by X-ray	32	69%

lengthened. In Table I is shown the survival rates at 3 years in patients treated with the combined treatment, and treated with X-irradiation alone. The survival rate is 69% for both groups. It is, therefore, unlikely that this combination is a beneficial procedure in Hodgkin's disease.

All of these compounds have a value in the control of *chronic lymphatic leukaemia*. They are less reliable in the myeloid forms and, in any case, there are a number of more reliable agents for treating myeloid leukaemia. In lymphoid leukaemia the results are good. I prefer TEM because of the ease of oral administration in patients who are often old and frail. Good results are also obtainable in these cases with TEPA and thioTEPA. In the choice of treatment in lymphoid leukaemia, the claims of splenic irradiation and of P.32 must also be considered since the effectiveness of these agents has been proved.

Few *epithelial tumours* show a response to these compounds. There is, however, a temporary beneficial effect in the advanced case of *carcinoma bronchus*. But the effects are not dramatic and they are not specific. It is doubtful whether the patients live any longer and there is seldom radiological evidence of improvement. About half the cases are symptomatically improved after HN2—such improvement as might follow palliative radiotherapy. The benefit in bronchial carcinoma seems to be more consistently obtained after HN2 than after TEM. This may be because the intravenous injection of HN2 yields a higher concentration in pulmonary tissue. Because of this possibility, efforts were made by Klopp and others to treat other solid tumours by injection into the artery supplying the region. Success has been very limited and the method has its dangers. We have injected TEPA into the carotid artery in a patient with a tumour of the brain. The man regained consciousness for a few days after each injection but the benefits were very transient. *Malignant effusions*, especially in the chest, can be controlled by the intrapleural injection of TEM or its analogues; this control is similar to that which is obtained by a similar treatment with radioactive gold.

Another solid tumour of doubtful pathology which shows a response to HN2 and to TEM is the *lymphoepithelioma of the nasopharynx*. The regression is temporary and less good than follows radiotherapy. There has recently been a report that thioTEPA is of value in some cases of advanced *breast cancer* (Bateman, J., 1955). We have not yet confirmed this but it might be worth while if radiotherapy or hormone therapy had failed.

Another compound of fairly recent origin is the sulphonic-acid ester 'Myleran'— $\text{CH}_3\text{SO}_2\text{OCH}(\text{CH}_2\text{CH}_2\text{CH}_2\text{OSO}_2\text{CH}_3)$  (Haddow and Timmis, 1953). This is one of many substances which were synthesized on the basis of a hypothesis to explain the oncolytic effects of the mustards. It was thought that their activity depended on their ability to cross-link the amino-acid chains of the chromosomes and so prevent cell division. The hypo-

thesis is not now thought to be correct, but the compound so evolved was found to be active and clinically useful in *myeloid leukaemia*. It is more selective than those I have just described, in that the main effect is on cells of the myeloid series. However, the depression of these cells is not limited to abnormal cells and hence it is possible, as with other chemotherapeutic agents, to damage the bone-marrow irreversibly. Because of its selective action the obvious field for this compound is the treatment of chronic myeloid leukaemia. It is useless in the acute forms and also in lymphoblastic and monocytic types. It is, however, a reliable and convenient drug in chronic myeloid leukaemia and should be considered as an alternative to splenic irradiation, to P.32 and to urethane, all of which are similarly valid. The dose of Myleran is adjusted by the response; it is given by mouth and there are few side-effects.

#### URETHANE

Urethane, or ethyl carbamate, was described as an antimitotic agent by Warburg, and it is not yet known exactly how it acts. It has been suggested that it interferes with nucleotide synthesis by forming a purine analogue which is useless to the cell and so inhibits mitosis (Roe, 1954). If this is so, it should perhaps be classed among the antimetabolite drugs which I shall describe presently. It is a simple substance (Fig. 3) and

URETHANE  
(ETHYL CARBAMATE)

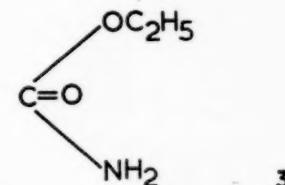


Fig. 3.

none of its derivatives seem to be anything like as effective in human leukaemia as the parent substance.

The main use of urethane is in the management of the *chronic leukaemias*, and it is about equally effective in the myeloid and in the lymphoid form. Oral medication can be given over a long period with excellent results.

The main use of urethane is undoubtedly in leukaemia, but there are a few solid tumours which respond to it. For example, *lymphoepithelioma of the nasopharynx* is sensitive to urethane. Since this lesion can be cured by radiotherapy, urethane treatment should only be used if radiotherapy is not available. This state of affairs may well obtain in the Orient, where the disease is extremely common. In such a situation urethane is preferable to the mustard type of compound since it is more effective. Urethane is also moderately successful as a palliative treatment in *multiple myeloma*—that most intractable of tumours. It certainly reduces pain and disability in some cases and I have found it rather more reliable than the many other chemotherapeutic agents that have been used in myelomatosis.

## THE ANTIMETABOLITE COMPOUNDS

The introduction of compounds which are generally called antimetabolites has opened a new approach to chemotherapy, particularly of the acute leukaemias. These compounds are very similar in structure to substances which the cell normally uses in building up its nucleoprotein; they differ from these substances in being useless for the purpose. The cell so cheated cannot divide. Fig. 4 shows, for example, the similarity

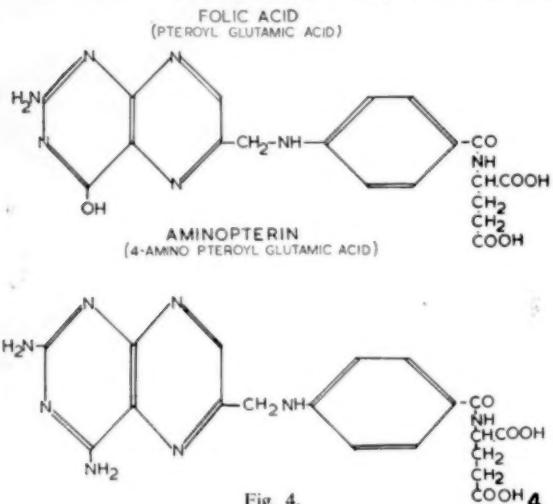


Fig. 4.

in the structure of folic acid and of the antimetabolite aminopterin. The leukaemia cell has a high requirement of folic acid, or rather of its active derivative, the citrovorum factor. If the cell is offered not folic acid but aminopterin, it will accept this substitute but, having done so, it is unable to proceed with division.

The antimetabolite drugs have made an important place for themselves in the management of the *acute leukaemias*, particularly in children. The antifolies, such as aminopterin and a-methopterin (Fig. 5) are not only a logical approach but a successful palliative measure. Their effects are slow and some patience is required at the outset. In the patient who is really ill, particular benefit is obtained by a treatment which combines an antifolic with one of the hormones, ACTH or cortisone.

The antipurine, 6-mercaptopurine, is another antimetabolite which can effect a dramatic improvement in acute leukaemia. The structure of the purine, adenine, and of 6-mercaptopurine is compared in Fig. 6. This compound blocks purine metabolism by substitution and it has a wider range of usefulness than the antifolies. It is excellent in acute leukaemia; it is also effective in *chronic myeloid leukaemia*, sometimes in the acute terminal stages; and it is occasionally useful in *monocytic leukaemia*. I do not think it should be used in chronic leukaemia with a reasonably good prognosis because, while it is effective, the disease relatively quickly becomes resistant to antimetabolites. It should therefore be reserved for the terminal acute phases of the disease, when it can extend life and comfort considerably after

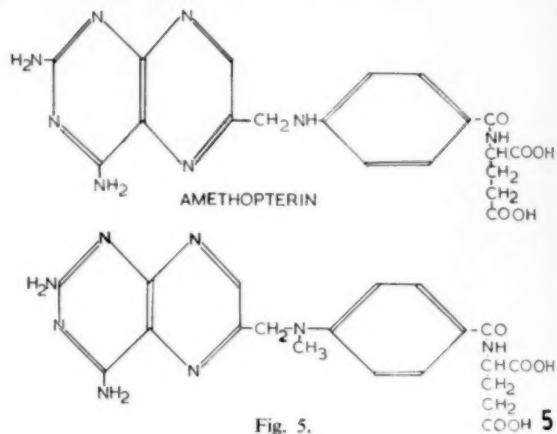
AMINOPTERIN  
(4-AMINO PTEROYL GLUTAMIC ACID)

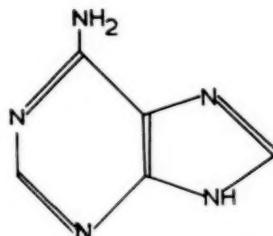
Fig. 5.

other treatments, such as radiation or the radiomimetic drugs, have lost their value.

Both these antimetabolites are of much greater effectiveness in children and young adults than in the older patient. The outlook for the child with acute leukaemia has changed very greatly with the introduction of these compounds and of the steroid hormones, and the expectation of life has more than doubled.

The antimetabolites must be used with very great care.

## ADENINE



## 6-MERCAPTOPURINE

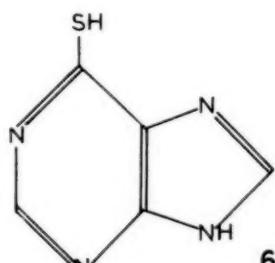


Fig. 6.

Both types of ulceration usually occur of the areas the good citrovorum to 6-mercaptopurine. These samples of action.

Pyrimidine antimetabolites. This compound and here the para-positions effective appears.

lesser blood platelets treatment compound native to cythamer to the drugs used.

At the stances be classified as anti-interfering properties malignant these compounds are radio-antimetabolites. concentrations are effective synthesis greater normal gerous tremely.

Other a cell by cells, for glycolic acid has approach. Some

Both types can be toxic and early toxicity is shown by ulceration of the mucosa of the mouth. Symptoms can usually be stopped by stopping the drug. In the case of the antifolies, the toxic effects on the patient and also the good effects on the disease can be reversed by giving citrovorum factor. There is, however, no clinical antidote to 6-mercaptopurine.

These antifolies and antipurine metabolites are only samples of a number of compounds with a similar mode of action.

Pyrimethamine, also known as Daraprim, is another antimetabolic drug of interest in a different field (Fig. 7). This compound was evolved for the treatment of malaria and here it undoubtedly acts as an antimetabolite to the parasite. At a higher dose level it is a reasonably effective treatment for *polycythaemia vera*. Daraprim appears to suppress red-cell production; it has also a

DARAPRIM

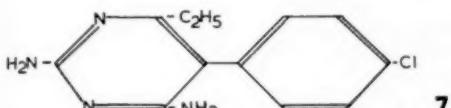


Fig. 7.

lesser but definite suppressive effect on white cells and platelets so that the size of the dose and the duration of treatment must be carefully watched. It is a fairly new compound but seems likely to take its place as an alternative to P.32 or TEM in the management of *polycythaemia vera*. Sooner or later it is likely that resistance to the drug will develop and other treatment must be used.

#### MODE OF ACTION

At the present day, most of the chemotherapeutic substances in clinical use, other than the hormones, could be classed perhaps rather roughly as radiomimetic, or as antimetabolic. They all inhibit cell-division by interfering with nucleic-acid synthesis, that unique property of living cells, whether they are normal or malignant. There is no reason to believe that any of these compounds so far described localize specifically in malignant cells. Most of them have been labelled with radio-active isotopes and have not been found in greater concentration in tumour tissue. Their activity when they are effective depends on the high rate of nucleic-acid synthesis in actively proliferating tissues and upon the greater sensitivity of the malignant cell than of its normal counterpart. All of them are potentially dangerous and require close supervision; they can be extremely valuable if properly used.

#### OTHER APPROACHES

Other attempts have been made to destroy the cancer cell by attacking more specific properties of malignant cells, for example their property of aerobic and anaerobic glycolysis. Such inhibitors as fluoride and iodo-acetic acid have been tested. In spite of the logic of this approach, the clinical effects have not been impressive. Some neoplasms such as myeloid leukaemia and Hodg-

kin's disease responded, but the solid carcinomas for which we lack effective agents did not (Black *et al.*, 1949).

Substances of vegetable origin have also been tested. There is at present a renewed interest in colchicine. This alkaloid from the autumn crocus is a powerful mitotic inhibitor and very toxic. Recently a colchicine derivative, diacetethylmethylcolchicine, has been found to be much less toxic and to be beneficial in myeloid leukaemia. Another substance of vegetable origin is podophyllin, derived from the mandrake root. It is also a mitotic inhibitor and its great toxicity was appreciated by the American Indians, who used it as a purge or a poison, depending on circumstances. It is still as toxic!

Recently the antibiotics have been, in part, explored for their effect on the cancer cell. So far I do not think that oil has been struck, but there is a certain interest in actinomycin, which was a forerunner in the series which gave us streptomycin. One of the actinomycins is said to have a beneficial effect in Hodgkin's disease.

These last compounds do not seem to open any promising avenues. Perhaps a more useful trend of thought is the idea of synergism between two active agents with different paths of action in the cell. This is a similar approach to the present-day treatment of tuberculosis, in which two agents given together have a greater arresting effect on the disease than either given alone. It is always difficult to say clinically that synergism has occurred in any particular case of malignant disease, but there is certainly an impression that in acute lymphatic leukaemia it is advantageous to combine an antimetabolite with one of the steroid hormones. Other attempts at synergism can be instanced. For example, there is the use of synkavit as an adjuvant to X-rays, as advocated by Mitchell.

It would be equally valid reasoning if we could combine a toxic chemical with a substance which would protect the normal body-cells. So far, I am not convinced that a suitable combination has been discovered, since most protective agents protect both host and tumour, although it is possible that subtle differences in protection may exist.

In spite of the clinically useful compounds that have emerged from the research of the last few years, we are still at the beginning of our exploration into ways of attacking the cancer cell by chemical means. One worthwhile investigation, to my mind, would be to seek out the nature of the resistance which develops in cells to the action of chemotherapeutic compounds, especially the antimetabolites. Such a study might lead to methods which would at least delay this occurrence. Perhaps the greatest need of today is research into the physiological mechanisms of the normal cell of any one tissue and of its malignant counterpart, for example the epithelial cell and the epithelioma. This would enable us to exploit with confidence differences in their vital processes, differences which may be very small.

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## THE LIMITS OF SURGICAL THERAPY\*

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Guy's Hospital, London

The surgical treatment of cancer is, at its best, crude, distasteful and only moderately efficient. We may well ask ourselves whether it is worth while embarking on it at all; and indeed we have some need to ask ourselves this question because in certain cancers, such as cancer of the breast for instance, there are those who maintain that surgery, however timely, however extensive, cannot prolong the life of the patient by so much as a day. This school which might take for its motto *omnia desperanda* has certainly caused a flutter in the dove-cotes, and like many flutters this one may be the prodromal manifestation of a panic flight. There are some signs that this is so for, like all panic flights, there is a scatter in different directions, and those who are left behind, quietly considering, before they move, in which direction safety may lie, find themselves isolated and even abused for being complacent and reactionary. The scatterers, on the other hand, have fled in two opposite directions. There are those who do less and less in the way of surgery and seek to rely on the hidden influences of X-ray therapy, the precise extent of which none can gauge, to cover their deficiencies; and there are those who regard this new conception as a challenge to their ingenuity, their dexterity and even their honour, so that they do more and more surgery in an endeavour to outflank an invasion which threatens to overtake and overwhelm them like waves following a sailing ship running before the wind.

To defend or attack the first school is not my present concern. At least it can be said for them that they appear to do little harm; they do not mutilate, and in dealing with other peoples' lives restraint is ever the better part of valour. Time may show that they have chosen the wiser course, but whether they were wise to choose this course before time has revealed their wisdom would be a matter suitably dealt with on a separate occasion. It is with the second school—that which claims that, if surgery be good, bigger surgery is even better—that I would deal to-day.

One of the protagonists of radical surgery in the treatment of cancer, wisely includes this prelude to a dissertation on the subject:

'In taking stock we should never champion a principle of treatment without consideration of the individual patient for whom it is intended. Is the indication for the radical mutilating operation a pride in one's technical capability or an actual need by the patient? Is it the principle or the necessity which dictates the choice of the operation? Shall it be a routine or an elective procedure? Is the human residue happy?'

If one may perhaps take exception to the application of the term 'human residue' to someone's well-loved mother, wife or child, one must applaud the sentiment and support the principle so clearly stated here. It is somewhat

\* A paper presented at a symposium on the Treatment of Carcinoma held in plenary session at the South African Medical Congress, Pretoria, October 1955.

worrying to read a little further on, albeit as a courageous confession of error:

'One may justifiably and ruthlessly remove multiple organs if the patient thereby is given a reasonable prospect of cure or a shorter life worth living. On the contrary, one of our patients with leukoplakia of the oral cavity, pharynx, larynx and oesophagus, developed multi-centric cancers and at intervals of years underwent glossectomy, total laryngectomy and finally oesophagectomy. It was a surgical triumph, even though he couldn't talk, masticate or swallow. He committed suicide.'

One wonders whether this outcome might not reasonably have been anticipated.

But to illustrate the principle one need not elaborate upon the declared confession of a great American surgeon and investigator; instead I should like to read to you words spoken at a meeting of the Society of University Surgeons in 1951:

'I wish to propose in all seriousness that pelvic exsection is not necessarily the most radical operation that you can conceive. Even if there may be fixation in the pelvis, involvement of the external iliacs or inguinal regions, there is still the theoretical possibility of operative removal by pelvic amputation, simply a halfectomy. Secure the terminal aorta and vena cava and the rest of the operation would be relatively simple. Simply divide the vertebral column, secure the dura, and what not.'

'May I have that slide, please. It is a horrible thought to be sure, but I have done this suprapelvic amputation on a cadaver and that would be the result. I believe you could fit a prosthesis on this and make a decent living individual. It was disappointing, though, when we put radio-active phosphorus in the embalming fluid in this cadaver, that the circulation in those flaps was rather poor. So you'd probably have to do this in two stages.'

## BREAST

If we consider the more reasonable application of the super-radical idea, there are certain branches of cancer surgery where these excursions into the peripheral fields of spread must be considered with respect. In the case of the breast, for instance, the work of Handley and others has shown that the internal mammary chain is not uncommonly implicated and it is a not unreasonable conception to seek to include this region within the parts ablated in a operation for cancer of the breast. Such a consequence of these pathological studies has been pursued by Urban, Wangenstein and others, who not only take away part of the chest wall including the internal mammary chain, but stray into the supraclavicular region and amputate the opposite breast almost as a routine in such cases. How far is all this justified? Certain it is that the mutilation produced is considerable and the immediate mortality, at least in average hands, would be increased; but life is precious and, within limits, a high price may properly be paid for survival. I think in regard to such measures, the wise course for the general run of surgeons is to adhere to what has served, however imperfectly, over the years and to modify our practice only when we know that something better is available. Certainly when the alternative carries a burden of mutilation and morbidity we must be very

sure before we abandon a well-worn and clearly-charted path for the rough-and-tumble of unexplored country. At the same time it is proper that these possibilities should be explored, but this exploration should be left to those well qualified to do so—qualified because of special talents, qualified in possessing an organized system for following up these patients, and qualified in the scientific assessment of the relation of cause and effect.

On the other hand we cannot ignore the implications of these pathological advances and we may equally profit by them although they do not tempt us to undertake heroic surgery.

The chances of internal mammary lymph-node involvement depend, as one might well expect, upon the site of the tumour within the breast. In tumours situated in the medial half of the breast, involvement of this group of glands is more likely; in fact in Stage-I tumours in the lateral half of the breast, internal mammary chain involvement is rare. This observation should be taken into account in planning our therapy. In growths of the medial half of the breast it is wise to explore the 2nd interspace in the region of the internal mammary artery and to remove for frozen section any gland which is found there. The 2nd interspace is chosen because if there is no involvement with growth in the gland of this interspace, involvement elsewhere is unlikely and it is therefore a good sample to choose. If frozen section shows involvement of this gland, it is obviously fruitless to proceed with radical mastectomy and simple mastectomy should be performed with radiation therapy to the lymph nodal fields. If this gland is found to be free from deposit then radical mastectomy is proceeded with. One might logically demand that this preliminary biopsy be performed for growths wherever they are situated within the breast, because it is not possible pre-operatively to say whether the axillary nodes are involved and, when they are, even laterally-situated primary tumours may be associated with involvement of the internal mammary chain. Nevertheless, unless this axillary involvement is clinically considerable, the chances that the internal mammary chain is involved in cases where the primary is laterally situated are remote; and in these cases the preliminary biopsy takes place within what will probably be the medial flap of the final operation and so tends to devitalize it. In medially situated growths, on the other hand, the biopsy wound will be included in the area of skin extirpated and no technical aggravations are added to the procedure.

#### STOMACH

In cancer of the stomach the classical method of treatment is subtotal gastrectomy. Nobody would care to claim that this operation is a satisfactory method of treating this condition; but if it does not prolong life, it makes this life in many cases more tolerable and improves its quality to an extent which alone makes the operation desirable, even obligatory. Because, however, of dissatisfaction with the ultimate effect of this measure, attempts have been made to 'improve' upon it. When the stomach wall at the upper end of the classical gastric resection specimen is examined histologically, even when the

growth was apparently confined to the pylorus, it is not uncommonly found that cancer cells are lurking in the submucosa. If this be the case, so the argument runs, let us take away the whole stomach and remove this possibly contaminated residue. Now by this simple extension of the operation a different world is created for the patient, indeed it may very easily be the next world; but if he survives in this, his comfort, his digestion, his nutrition and his composure are jeopardized to an extent which demands that we should be very sure of a profitable return in respect of survival rate in exchange for such a considerable price. In fact this return is negligible, and it has happily been a matter of only a few years before it has been shown that the chances of survival are not improved by the performance of total gastrectomy for pyloric cancer, and in the meanwhile the patient is likely to be rendered dyspeptic, wasted, flaccid and unhappy.

To adopt a conservative attitude towards the extent of our operation upon the stomach is not to say that we shall be conservative in our attitude towards the indications for its performance. Thus secondary deposits within the liver are no contra-indication to subtotal gastrectomy, which in any event is almost always but a palliative measure. Indeed, with improvements in technique the removal of one or two secondaries from the liver—if this is all that can be found—is a procedure which adds nothing to the burden the patient has to bear and may—who knows—contribute towards his comfortable survival. Recently indeed we have heard of removal of whole lobes of the liver, the right as well as the left, and those who have performed this operation claim that it is technically easier to do this than to take pieces out. With adequate control of the respective branches of the hepatic artery, portal vein and hepatic duct this may indeed be the case and, if this operation proves to have a tolerably low mortality, it may well be a matter for serious consideration in the future.

#### RECTUM

Reference has already been made to the horrible possibilities of the logical extension of the operation of pelvic evisceration. What of this operation itself? Experience with the consequences enjoins caution in any out-of-hand condemnation of procedures which, for reasons perhaps largely emotional, are distasteful. At its inception complete pelvic evisceration demanded the burden of a 'wet colostomy', and this atrocity might well have relegated the operation to the objectionable, even the unthinkable; but surgical ingenuity has devised the artificial bladder fashioned out of a loop of ileum, by which contrivance the operation of pelvic evisceration may be well supported, and life rendered endurable. As more experience is gleaned with the ileal bladder it is clear that 'ileal' is no synonym for 'ideal'; this innovation creates inherent difficulties and problems. However these technical difficulties may have been ironed out, one must remember that total pelvic evisceration carries a mortality of 12 out of 65 even in Brunschwig's hands, and of the 53 survivors 34 lived only a few months and it was doubtful whether any palliation had been achieved. In 19 it is

claimed that there was effective palliation, but it must be remarked that only 7 out of the whole 65 survived more than 1 year and 5 months after having been subjected to this truly mammoth surgical procedure.

In the same way the discovery of oesophageal speech has robbed the operation of laryngectomy of much of its horror. If therefore we are inclined to adopt a middle path in our practice, we must be careful not to erect walls along the edges of this path so high that we are unable to see what is going on beyond. Some of these activities in the unexplored fields alongside may be but the antics of exhibitionists, but others might be the careful cultivation of ideas by thoughtful husbandmen, and it would be folly to condemn by prejudice the planting of a seed which might bring forth an abundant crop.

If we shy from the consequences of pelvic evisceration—when boldness is needed and with modern advances there is really no reason why we should do so in suitable cases—there is one situation where surgery must be bold to the point of recklessness: I refer to advanced carcinoma of the rectum with attachment to surrounding structures. To leave a patient in this condition without removing the primary is to condemn him to the likelihood of great misery. The growth will fungate into the perineum with the formation of fistulae. Similar fistulae may appear in the hypogastrium and these loathsome complications will add to the horrors of a perpetual bloody incontinence and the racking pain of nerve-plexus involvement.

Nowhere is the plea of Ogilvie more apropos—"If I have a cancer give me a surgeon with plenty of courage, a deal of dexterity and not much sense." In this condition the surgeon must settle down to a laborious, difficult and troublesome dissection without thought of his future engagements, his next meal or the long-anticipated solitary performance of his favourite orchestra. His duty is to get the growth out, and he cannot stop until he has done so. That these attempts may blot the copybook of his hitherto low mortality-rates is of little consequence. Nor is the performance of a 'palliative' colostomy an easy way out; it may get the patient out of hospital alive and the surgeon's reputation in the town remains unsullied, but he should visit the patient regularly afterwards as the family doctor has to do. He should sample the odour of faeces and pus which pervades the house, perhaps for months, and he should sit by the patient and see at first hand what he has done.

Many years ago I was guilty of this pusillanimity. Two patients with carcinoma of the rectum were on my list for operation in the same morning. It was soon after the war and my experience of these conditions, at that time by no means extensive, was rusty from disuse, I having been for the previous 5 years occupied with a practice in which carcinoma of the rectum was not considered. The first patient was a psychopath from our mental wards. The operation was difficult and tedious, the growth being stuck to surrounding organs and tissues. Nevertheless by dint of great perseverance and with much hesitancy I managed to get the growth away. At the conclusion of the operation I thought to myself: 'Here is the touchstone; this is the limit of my capabilities. In future if a case appears less difficult than this I shall

tackle it with confidence; if more difficult, I will leave it alone and content myself with a palliative colostomy.'

Having come to this profound conclusion, I was faced with the next patient. This was a lady in her late thirties. Her doctor had treated her diarrhoea of one year's duration as a 'dyspepsia' due to war-time food. She was the mother of 3 children, a gifted musician, beloved by her family and a wide circle of friends. When I opened the abdomen I saw to my horror that the growth was very fixed, involving coils of small intestine, inseparable (or so I thought) from the iliac veins, involving the uterus and attached to the sacrum. Almost with a sense of relief I found a secondary deposit in the liver. Without much consideration I performed a transverse colostomy.

At the time I was living a little way out of London and this lady's home lay but quarter of a mile from the road I used to take daily to and from hospital. Two or three times a week on my way home I called in to see her for a talk, and for 6 months I watched the relentless process of physical dissolution. The piano, which had been brought down to the ground floor where she lay in bed, at first provided solace; but soon she felt too tired to sit at it, and later too weak even to reach it. The fistulae which developed meant that this fastidious lady lay perpetually within a half shroud of malodorous wet dressings; and at the end she disliked the prospect even of her husband's visiting her, a husband to whom she was devoted, because of the distress which her pitiable plight occasioned him. Mercifully she lived only six months, dying quietly of jaundice and liver failure. Before she died she said to me, 'I know you did your best, but I wish to God you had killed me; this last 6 months have been the most miserable of my life—too miserable really to be endured.'

Had I done my best? I know now that I had not. My first case that morning is still alive and well enough to go in and out of lunatic asylums as his mental condition demands. If I had really set to work on the second patient, I might not have made much difference to her period of survival, but at least those 6 months which proved 'too miserable really to be endured' would have been calm, filled with music, sweetened by family love and attention, and a not unseemly prelude to a merciful death from liver failure.

—'Palliative colostomy'—there's no such thing.

#### MOUTH, OESOPHAGUS, PANCREAS

Recently the practice of simultaneous bilateral block-dissection of the neck has been advocated for extensive growths of the tongue and floor of the mouth where there is bilateral lymph-gland involvement. The idea behind this operation is that the growth and its ramifications must be removed 'en bloc', and in order to achieve this the most extreme trauma is inflicted upon the patient's anatomy and physiology. The simultaneous obliteration of both jugular veins demands a previous tracheotomy to overcome the laryngeal obstruction from oedema. The circulation to the brain receives the grossest insult and there is a temporary and occasionally a permanent and considerable disfigurement. It is doubtful indeed whether this operation can ever be justified in the

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face of the alternative methods of treatment which are available.

Finally, there are certain organs such as the oesophagus and the pancreas where a considerable degree of virtuosity is required even to remove the primary tumour, however little extension there may be. These operations are a trial to the patient and the mortality is considerable, so that it will be necessary to subject the indications for their performance to very critical scrutiny.

In carcinoma of the oesophagus we have these facts to consider: Untreated, the condition is rapidly fatal; untreated, too, the burden of dysphagia and inanition provides an unpleasant prelude to death. The simple palliative measure of gastrostomy is most burdensome and the insertion of a Souttar's tube so uncertain that it is only in a few cases that much profit accrues to the patient from the adoption of this simple and harmless procedure. In these circumstances the surgeon has a very free hand; there is little chance that he can make the patient's already distressing condition worse, and if the patient dies the unsought benefits of euthanasia are not unwelcome.

Before advances in anaesthesia, a proper understanding of electrolyte balance, and improvements in surgical technique, made surgical attack on the oesophagus a possibility, it was thought that if only these difficulties could be overcome the final results of oesophagectomy would yield a handsome dividend in terms of cure. Here was a squamous-celled carcinoma in a narrow tube, so that timely notice would be given of the existence of the disease, and pathological studies at post-mortem had suggested that spread to inaccessible parts was probably late. Alas! this conception could not be sustained as a result of experience. The survival rate after resection of the oesophagus for carcinoma is deplorable, and some surgeons now only aim at palliation as the goal in operating upon these conditions. Nevertheless, the burden which the patient has to assume when subjected to a palliative operation for carcinoma of the oesophagus differs so little from that following eradication or attempts at eradication, and the necessity for palliation is so urgent, that in this disease the surgeon may be said to have a *carte blanche* to go ahead and do what is necessary and possible.

In carcinoma of the pancreas similar considerations apply. Before such a thing became possible it was thought that removal of the pancreas would be a most effective method of treatment. Here again a lesion in or alongside a narrow tube giving rise to obstructive jaundice soon after its appearance would give early indication that something was amiss, and would provide a splendid opportunity for eradication before spread had occurred to inaccessible regions. Here again the necessity for palliation was paramount. Progressive jaundice and pruritus rendered the untreated patient's condition miserable; here again the performance has belied the expectancy.

How are we to deal with this paradox? I cannot do better than quote Rodney Smith who, in my country, has given careful consideration to these problems and whose great manual dexterity is tempered with a mature judgment. Firstly he would counsel that all cases should be explored unless manifest secondaries have

made the diagnosis beyond all doubt. In other cases there is always the possibility of mistaking a stone impacted in the ampullary region for a carcinoma, and the chance of curing a patient may therefore be ignored if absolute reliance is placed upon a clinical diagnosis. Where laparotomy is undertaken, and here I quote,

'It is the writer's belief that if a carcinoma of the head of the pancreas is found, the duodenum should be mobilized and before any irrevocable step is taken an estimate made not only of the extent of malignant invasion, but also of local oedema, fixity due to low-grade inflammation and the state of the rest of the pancreas. Unless the growth qualifies for excision under the stringent conditions already put forward, the surgeon should content himself with a palliative operation. Once every 5 years he may miss a 3-year cure, but against this he must set those patients whom he would have killed had an unwise attempt at resection been made, some of whom may have had as much as a year or more of comfortable life.'

The position is somewhat different in the case of an ampullary growth. Here a very real chance of prolonged, even indefinite, survival does exist. Illingworth (1951) goes as far as to say that more than half of those who survive operation may be expected to achieve a permanent cure. This may be putting the chances in a rather over-favourable light, but Cattell (1949) claims 25% of cases alive and well after 5 years, and one must be ready to risk a good deal for the sake of results of this kind. The immediate mortality, too, is a good deal lower than in radical resections performed for carcinoma of the head of the pancreas. It is true that the pancreas itself may still be the site of chronic inflammatory changes if the pancreatic duct is blocked, but the freedom of the peripancreatic planes from fixity or oedema allows the important relations of the gland to be clearly dissected and displayed and accurate haemostasis to be secured. The actual operative technique is, in fact, very much easier.

There is one doubt which must be expressed in considering the place of the radical operation in ampullary growths, and that is—would equally good results be secured by a conservative resection? There is no doubt that a case can be made for retaining the conservative operation of transduodenal resection in selected cases, though it is probable that the long-term results of the radical operation will prove to be rather better. It is impossible to be dogmatic on this question, but the present feeling of the writer is that the operation of choice in a patient the wrong side of 70 with a small ampullary growth, particularly if it could conceivably be innocent, is a trans-duodenal resection.

To summarize, then, a suggested plan for the selection of operation:

(1) If secondaries are present, resection is contraindicated. A palliative short-circuit of the obstructed bile duct is performed and, if duodenal obstruction appears likely, which is rarely the case, a gastro-jejunostomy as well.

(2) If no metastasis is present:

(a) Carcinoma of the head of the pancreas calls for mobilization and careful examination. Palliative short-circuit will usually be chosen, even in some cases technically still operable. Radical pancreateo-duodenectomy will be reserved for a very limited class of case.

(b) Carcinoma of the ampullary region will usually be treated by radical pancreateo-duodenectomy, but in patients over the age of seventy with a small tumour, trans-duodenal resection is preferred.'

#### EXCISION OF SECONDARIES

When discussing carcinoma of the stomach we saw that gastrectomy was not necessarily contra-indicated even when liver secondaries were present; indeed it was sometimes justifiable to remove these secondaries. Are there any other secondaries where removal may be contemplated? In this connection we must be careful to observe our principle that in dealing surgically with extensive malignant disease we must not make the

patient's present condition worse when the possibility of survival is so slight. Nevertheless, and bearing these stringencies in mind, there are two sites where solitary metastases may be excised with manifest profit to the patient's happiness and a possible return in increased expectancy of life; these are the lung and the brain.

Certain neoplasms, such as some hypernephromas, themselves slow growing, shed equally dilatory secondary deposits, and it is not uncommon in this disease for a solitary, slow-growing secondary, producing a 'cannon-ball' shadow on X-ray, to appear in the lung. In such circumstances it is both prudent and good doctoring to explore very carefully the possibilities of lobectomy or pneumonectomy, and where this has been done there are reports accumulating of satisfactory issues prevailing up to 10 years and more.

Some years ago a doctor's wife came to see me with a lump in the region of the shoulder-joint. I excised this and the microscopic report came back, 'malignant synovioma'. For some years this lady lead a normal symptom-free life but eventually a mass of glands appeared in the same axilla, and these were excised and found to be infiltrated in the same way. Shortly after this she developed intolerable headaches, vomiting and papilloedema. A secondary on the brain was diagnosed and craniotomy advised. This operation, performed by Valentine Logue, revealed that the secondary was solitary and it was removed. The patient was discharged from hospital in a fortnight. She came to see me a week later and, I should have thought most unwisely, accepted a glass of sherry, and had no more trouble from this complication for the next 2 years when she died of multiple secondary deposits.

#### CONCLUSION

How then may we summarize our attitude to these problems? One point has not been touched upon, namely relative skills. All of us in this hall are qualified surgeons, but we are not equally qualified. Where Cattell might remove a pancreas with impunity and satisfaction, I could only do so overburdened by tribulation and harassed with anxiety; where Keynes might extirpate the thymus from a patient in whom the advent of death would only constitute an imperceptible advance in his degree of myasthenia gravis, I would not care to tamper. No, it is an indisputable fact that most of us are average. We may have aspirations and these aspirations are excellent and to be encouraged. With the exceptional the fulfilment of these aspirations is a necessary ingredient for surgical advance. But if many of us are not exceptional we should, as qualified surgeons, possess exceptional common sense, and we cannot in these difficult considerations do better than refer back to first principles. Would I in these circumstances wish this upon my wife, upon myself? We may many of us interpret this maxim somewhat differently in given circumstances; but if we adhere to it in our consciences we shall not go far wrong and, above all, the great human family who entrust their lives and their happiness to our hands will be justified in that extreme confidence which it is, as medical men, ever our wonder and our satisfaction to observe.

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## CARCINOMA CERVIX UTERI—TREATMENT PRIORITIES\*

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The treatment of cervix cancer is important because it attacks a relatively young age-group, but even more because in the early stage it is, except for cancer of the skin, the most curable of all the common cancers. This fact is not as fully appreciated as it ought to be, but it is a statement well-supported statistically. Cancer of the cervix is the one disease about which, thanks to Heyman of Stockholm, we have world statistics. Table I shows for early cancer of the cervix (Stage I and II) the results of radiotherapy from a very large group of hospitals in many parts of the world, as collected by Heyman in his League of Nations and later reports. The number of patients concerned is large, and so these results cannot be due to selection of a few favourable cases, and the follow-up is complete so that the cure rate is genuine. Over 15,000 cases are alive over 5 years. This compares favourably with the cure rates published

for any large number of cases of cancer in any form. Detailed analysis shows in addition that steady improvement has taken place year by year. We will come to that later.

TABLE I. CANCER OF UTERINE CERVIX  
5-Year Results from 63 Centres in different parts of the World.

Stage	Number Treated	Number Alive	Crude Survival Rate
I ..	10,582	6,214	59%
II ..	23,190	9,268	34%
Total ..	33,772	15,482	46%

What has caused this improvement? I think it is the result of a combination of factors:

1. The public in many countries is becoming more conscious of the vital importance of early treatment.
2. New methods of early diagnosis are being developed.

\* A paper presented at the South African Medical Congress, Pretoria, October 1955.

3. Treatment is being improved, particularly in regard to calculation of dosage.
4. The risks of treatment are being eliminated.

I propose to study with you certain aspects of each of these factors.

#### EARLY DIAGNOSIS

It is now well known that early diagnosis and consequent early treatment are the secret of the high cure-rates of cancer in any site. It is particularly true for cancer of the cervix. All workers in this field are in complete agreement that great advances could be made were it possible to alter the outlook of ordinary people. We have to teach them something of the signs and symptoms of this cancer, but before we do so we have to teach them not to be afraid to seek advice as soon as these signs appear. Although we all believe that it is necessary for this information to be imparted, there are differences of opinion about the best way to bring it before the public, for propaganda has been much abused in the modern world and its effects are not always those expected.

Great efforts have also to be made to improve the education of the general practitioner in this respect. If he is careless or forgetful, he too can contribute to the delay.

The Scandinavian countries lead the world in the treatment of uterine cancer, not only because their technique is good, but also because they have induced a much higher proportion of their patients to seek advice early.

#### Diagnosis by Vaginal Smear

An addition to the technique of early diagnosis is diagnosis from vaginal smears—a technique devised and developed by Papanicolaou. It is much used—and abused—in the USA. What is its real value? It is, I believe, a very useful screening test, but it must never be made an exclusive basis for treatment. Where positive it must be confirmed histologically by true biopsy. Where negative it must not be regarded as excluding cancer in the face of suggestive symptoms. A vaginal examination at the right moment remains, therefore, the most important single item in the early diagnosis of this cancer, and far more important than all the laboratory tests in the world.

#### PROBLEMS OF TREATMENT

Propaganda and early diagnosis give opportunity, but in the end success depends on the method of treatment. On this subject there is still considerable discussion and some controversy. Is surgery or radiotherapy the better method or is a combination of the two more effective? How should radiation be given and, in particular, what is the place of X-ray therapy, either added to radium or as intra-vaginal treatment in its own right? Can methods based on the use of isotopes be developed to improve on the existing radium techniques? These and many similar questions await an answer, and considerable work is being done on all of them.

The topical question today is undoubtedly the choice between surgery and radiotherapy, or their judicious combination. I am going to say at once that I am

strongly of the opinion that for *cancer of the cervix* radiotherapy *alone* can give better results than surgery. It is not for me to discuss the technique of surgery or to deny that surgery may cure a few radio-resistant cases in which radiotherapy would have failed. The essential point is that radiotherapy will not only cure more early cases than surgery but also cures a considerable proportion of cases which are already inoperable. The main argument against surgery is related to the direction of local extension from primary cancer of the cervix. It is well known that the first line of spread of a cervical cancer is laterally on to the fornices, and then into the base of the broad ligament. There is no need for me to remind you of the anatomy of this region, or of how close this site is to the ureter as it passes forward to enter the base of the bladder. Once the tissues near the ureter are involved, the need to separate the ureter from the vessels and preserve it makes it almost certain that malignant tissues will be cut into. Such a process is against all the principles of reliable surgery for malignant disease, and so limits results. In contrast, cancer round the ureter is well within reach of full doses of radiation from intracavitary radium and may thus be destroyed by radiotherapy even without additional X-ray therapy. It is this weakness of the older surgical approach which has led to the recent craze—I use the word deliberately and perhaps provocatively—for more radical operations with ureteric transplantation. The morbidity from these is almost worse than the number of cases radiotherapy fails to cure!

In favour of surgery it is often claimed that secondary deposits in lymph-nodes cannot be cured by radiation. I admit at once that it is doubtful whether the older forms of radiotherapy cured many cases of secondary squamous-cell cancer in lymph-nodes; but present day methods do cure some. In the cases proved to have deposits in pelvic nodes from cancer of the cervix, it seems to me that surgery does not cure many either. A number of groups of surgical cases have been published showing the incidence of node involvement, but very few show results at 5 years of the treatment of these cases.

The relative safety of modern operating is not disputed, but, even so, the Wertheim operation is an ordeal not without some mortality. Why then use it when another and better method of treatment is available, and is infinitely easier for the patient?

If all this be true, why then have we seen the recent swing-back in the USA towards some form of surgery in this disease. I think there are many reasons for this but they all amount in some form or other to a comparison between the surgery of *today*, with all its modern assets, and the radiotherapy of *yesterday*—totally oblivious of the fact that in many countries radiotherapy, too, has advanced *pari passu*. Indeed, nowadays the only excuse for surgery is that in the centre involved the radiotherapy is bad.

When I talk of the radiotherapy of *yesterday* I am tacitly admitting that radiotherapy as practised 10-20 years ago was *not* all that it ought to be. Many blemishes in actual practice might be mentioned, but the main ones were:

1. Even when nominally according to a standard method, such as the Stockholm technique, treatment was often in practice most haphazard and casual.

2. Post-treatment sepsis was a serious complication.

3. High-dose effects, with fistulae in the worst cases, did occur.

4. X-ray treatment, if added at all, was planned on altogether the wrong lines.

5. Dosage was in terms of milligram-hours of radium used. This does not really measure dose and so can be very misleading.

At a recent radiological congress I pointed out how the passage of the years has seen each one of these defects corrected. May I recapitulate here the points I made at that time, as they seem entirely pertinent to this discussion.

*The casual approach to treatment* I put first because it used to be very prevalent. Radium was regarded as a superior kind of diathermy. Far, far too often it was considered technically so simple that it was left to junior medical staff. The mere presence of some radium inserted anyhow into uterus or vagina was ranked as acceptable treatment. Even the number and duration of insertions had often no consistent basis. It was, I think, first demonstrated irrefutably by Dr. Hurdon at the Marie Curie Institute in London, that a meticulous technique could yield real profits. She was a master of detail, pre-operative and post-operative, as well as in the actual insertion and positioning of the applicators and tubes. Using the standard Stockholm boxes, but with a perfection of technique and hospital care, she lifted the over-all 5-year survival to over 40%, long before anybody else did so. Heyman's successor, Dr. Kottmeier, too, lays great stress on this question of technique, and on the value of experience with adequate numbers of cases for those selected to control this method of treatment.

*Septic complications*, including peritonitis, could be minimized by special care in nursing, but right up to the advent of modern chemotherapy, even in the best centres they remained a major anxiety. Since then this complication has practically disappeared. The radium treatment of the average case of carcinoma cervix now carries a negligible mortality and morbidity equally for radiotherapy as for surgery. Moreover, because of this, from the patient's point of view the course of radiotherapy has become remarkably simple in its freedom from discomfort, risk, or immediate after-effects.

*The incidence of necrosis and high-dose effects* in the old days presented a similar problem. It is important that we as radiotherapists should admit in retrospect how serious a complication this was at one time. It can only be totally eliminated by underdosage and inadequate therapy. As this would be futile, we must seek ways by which its incidence may be kept at minimal levels. Today, where carefully controlled radiotherapy is practised the incidence of serious necrosis is low and it should, indeed, become even less common in the next two or three years. Its elimination is partly related to the general improvement of treatment technique, which I have already mentioned. It is also due to immediately post-operative radiographic control of the radium to verify correct and safe positioning. A further valuable safeguard, which

ought to become universal, is the direct rectal dosimetry which is employed in a number of centres, by means of scintillation counters.

The diminishing incidence of necrosis is, however, also partly due to the new conception of dosage to which I will refer later.

*X-ray treatment* as an adjuvant to radium has steadily improved. In the beginning, if used at all, it was almost universally applied as 'large fields' to the whole pelvis. There was no realization of the modern principle of radiotherapy that the factor of 'volume irradiated' has almost as much bearing on results as the 'time factor'. This principle can be stated as follows: the smaller the volume irradiated, provided the tumour-bearing zone is covered, the better the results. The more old-fashioned approach to whole-pelvis irradiation, generally with multiple fields of the order of  $10 \times 15$  cm., has gradually been modified to some form of accurately beam-directed technique aimed at the lateral parametria only, and sparing the already irradiated central zone. Megavolt therapy in any form, including cobalt beam units, has been shown to be of great assistance in achieving this purpose elegantly, but is by no means essential. We now know that the maximum dosage that could be given by the large-field method could scarcely ever have cured lateral pelvic nodes and its use only paid lip-service to this aim. With the principle of small field and small volume, the summated radium and X-ray dosage in the region of the obturator gland is substantial and probably controls the small-node metastasis in just as many cases as does pelvic surgery.

To these changes, which are fairly generally accepted, should be added two others of importance concerning dosage, initiated by the late Dr. Margaret Tod of Manchester. The contributions which I have in mind are the method of measuring treatment in terms of true tissue-dose in roentgens instead of ray-hours, and the establishment thereby of some knowledge of optimum dose. The whole scientific basis of any branch of radiotherapy is strengthened when we begin to think of dosage in terms of the radiation absorbed at the tumour and not merely as connoted by some measure of the size or strength of the radiating sources. It is, therefore, entirely fair to credit the original cervix dosage-system set out by Tod and Meredith (1938) as a substantial advance. It has recently been revised and 'streamlined' under the title of the 'Manchester Technique' (Tod and Meredith, 1953).

A true dosage-system such as this, however, does more than permit us to reproduce our treatments. Its greatest value lies in the fact that it can lead us in time to knowledge of optimum dose. The details of this study have been published—Tod (1941 and 1947), Paterson (1952).

If all these things have resulted in real advance, they ought to be demonstrable statistically in steadily improving results. Statistics show that this really is the case, and that it can be equally proved from Heyman's world statistics, or from the study of one individual centre such as my own hospital in Manchester. Tables II and III show figures culled from Heyman's League of Nations and subsequent reports. Table II is a simple over-all summation of the reported results. It shows the definite advance made between 1926 and 1945 even

TABLE II. CERVIX CANCER: HEYMAN REPORTS—ALL CENTRES

Years	Number Treated	% Well 5-years (Crude)
1926-30 ..	6,287	26%
1931-35 ..	12,124	29%
1936-40 ..	18,536	32%
1941-45 ..	24,156	36%
1946-47 ..	12,521	38%

as evidenced by summated world statistics, running into so many thousands that there can be no question of selection or bias. The striking thing about this table is the steady improvement over the last 2 decades. This is interesting because there has been in that time no great change in basic principle of treatment. The Stockholm and the Paris methods, either in their original form or in one of their modernized versions, still dominate

TABLE III. CERVIX CANCER: HEYMAN REPORTS—10 BEST CENTRES

Years	Number Treated	% Well 5-years (Crude)
1926-30 ..	2,925	27%
1931-35 ..	4,604	33%
1936-40 ..	5,985	38%
1941-45 ..	7,235	43%
1946-47 ..	3,095	44%

treatment. The improvement must, therefore, be related not to new principle but to technical advance and to better application. Such mass figures, however, summate the work from both good and poor centres. What is really possible today—and easily possible—is shown most strikingly in Table III, which shows the results of the 10 best centres in the various reports—an advance of no less than 16% in under 20 years. Note that the figures are still in terms of thousands of cases and not selected handfuls. I do not want to lay any particular stress on

TABLE IV. TREATMENT OF CERVIX CANCER

Years	Number Treated	% Alive 5-year
1933-38 ..	921	28%
1939-44 ..	1,671	36%
1945-47 ..	1,033	40%
1948-49 ..	690	42%

our own work in Manchester, but any speaker should be able to back up his statements from his own experience too. Table IV is given, therefore, to underline that what is happening on a world scale is also demonstrable for one individual centre with no change in the kind of material presenting, and certainly no change in the average stage of disease.

These are all 5-year figures of what *has been* achieved. The legitimate presumption is that the work of today is even better. There is indeed some evidence that this is

so in the vital statistics of the more advanced countries. In England and America, the death rate from this disease has come down to some 75% of what it was 25 years ago. In Scandinavian countries, this figure may well be higher.

*At this point a number of slides were shown illustrating various facets of the Manchester technique.*

#### DISCUSSION

We must not stand still, and our last question becomes, 'Where do we go now?' It is never easy to envisage the future, but we can, I think, find some suggestive indications. I have been putting emphasis on the value of present-day radiotherapy on its own, yet there are some radio-resistant cases. A well-conceived attempt to devise scientific methods of isolating the resistant case is in train in Boston, using Ruth Graham's criteria of radiation response. This is a promising line of investigation, provided one remembers that it is still an experiment and not a proved entity.

Even without it, however, I feel that greater use should be made of surgery as the second line of defence in failed or failing radiation cases. After all, if I may reverse an argument previously used, surgery has advanced *pari passu* with radiotherapy and is infinitely safer than it was. I believe that it does not help to apply it as a routine post-radiation adjuvant in *all* cases. This second-line-of-defence argument is, of course, not entirely palatable to the practising surgeon or gynaecologist but, after all, it is already the established way of things for mouth cancer—and to a lesser extent bladder cancer—so why not cervix?

TABLE V. CERVIX CANCER: HEYMAN REPORTS—10 BEST CENTRES: EARLY-LATE COMPARISON 1941-47

Years	Number Treated	% Well 5-years (Crude)
Early ..	6,495	54%
Late ..	3,823	25%

The other way in which advance could undoubtedly be made is by expansion of our efforts to get both patient and doctor to act on the early symptoms of cancer. Perhaps that way as much could be done as by any purely technical advances. How much this could be is well emphasized in Table V.

The main point to remember is that this is one of the diseases which it is infinitely satisfying to treat because it is, by and large, one of the more curable cancers.

#### REFERENCES

Paterson, R. (1952): Brit. J. Radiol., 25, 505.  
Tod, M. C. (1947): Acta radiol., 28, 564.  
*Idem* (1941): Brit. J. Radiol., 14, January.

#### UNION DEPARTMENT OF HEALTH BULLETIN

*Union Department of Health Bulletin.* Report for the 7 days ended Thursday 8 December 1955.

*Plague:* Nil.

*Smallpox: Cape Province.* One (1) European case in the Cape Town municipal area.

*Typhus Fever: Cape Province.* One (1) Native case in the Port Elizabeth municipal area. Diagnosis confirmed by laboratory tests.

One (1) Native case in the Matatiele district. Diagnosis confirmed by laboratory tests.

*Epidemic Diseases in Other Countries.*

*Plague, Cholera, Typhus Fever:* Nil.

*Smallpox* in Rangoon (Burma); Phnom-Pehn (Cambodia); Allahabad, Kanpur, Madras (India); Dacca (Pakistan); Tanga (Tanganyika).

## THE SURGERY OF INTRATHORACIC MALIGNANCY\*

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The purpose of this communication is to describe briefly the classification, incidence and surgical treatment of intrathoracic malignancy based on consultant thoracic practice in private, at the Johannesburg General

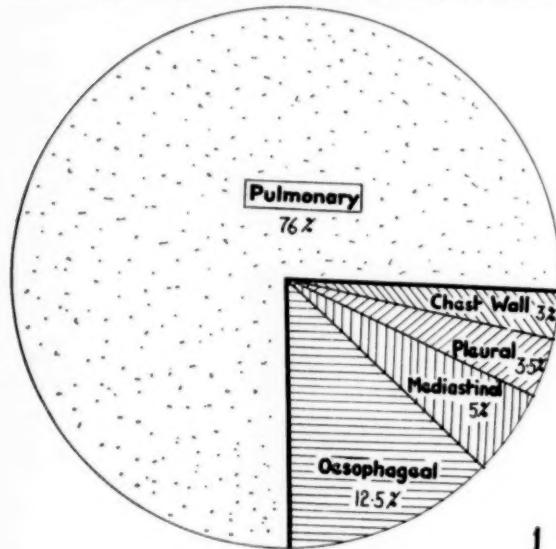


Fig. 1. Thoracic malignancy: 636 cases

Hospital and at the Thoracic Units attached to the Department of Surgery of the University of the Witwatersrand. A series of 636 cases of intrathoracic malignant disease is analysed, recorded from January 1947 to December 1954 as regards private cases, and January 1950 to December 1954 hospital cases.

## CLASSIFICATION AND INCIDENCE (FIG. 1)

		Cases
I. Pulmonary malignancy (Fig. 2)	Primary	483
A. Primary		429
1. Bronchogenic carcinoma	(a) Squamous-cell carcinoma	420
2. Bronchial adenoma	(b) Large-cell carcinoma	6
3. Alveolar-cell carcinoma	(c) Small-cell carcinoma	1
4. Lymphosarcoma	(d) Adeno-carcinoma	1
5. Haemangio-endothelioma		1
B. Secondary pulmonary metastases (Fig. 4)		54
II. Pleural malignancy (Fig. 5)	Primary	22
A. Primary		2
1. Pleural endothelioma		1
2. Fibrosarcoma of pleura		1
B. Secondary (pleural effusion)		20

\* A paper presented in a symposium on the Treatment of Carcinoma held in plenary session at the South African Medical Congress, Pretoria, October 1955.

III. Carcinoma of the oesophagus	..	..	80
IV. Mediastinal malignancy	..	..	32
A. Primary (Fig. 6)	..	..	15
1. Thymic	(a) Lympho-epithelioma	..	9
(b) Variegated carcinoma	..	1	1
(c) Lymphosarcoma	..	4	4
2. Miscellaneous	(d) Rhabdomyosarcoma	..	6
(e) Reticulum-cell sarcoma	..	1	1
(f) Neurofibrosarcoma	..	1	1
(f) Giant follicular lymphoblastoma	..	1	1
B. Secondary	..	..	17
1. To the reticulos, Hodgkin's disease, etc	..	..	7
2. Glandular metastases from carcinoma	..	..	10
V. Chest-wall malignancy (Fig. 7)	..	..	21
A. Primary	..	..	6
1. Ewing's sarcoma of rib	..	2	2
2. Chondrosarcoma of rib	..	1	1
3. Fibrosarcoma of rib	..	1	1
4. Fibrosarcoma of diaphragm	..	1	1
B. Secondary	..	..	15
1. Direct invasion	..	..	9
(a) by carcinoma of bronchus	..	4	4
(b) by Hodgkin's disease	..	1	1
(c) by carcinoma of breast	..	4	4
2. Haematogenous spread	..	..	6
(a) in multiple myelomatosis	..	3	3
(b) in carcinoma of prostate	..	3	3

## I. PULMONARY MALIGNANCY

## A. I. PRIMARY BRONCHIOGENIC CARCINOMA

We have seen 420 cases of bronchogenic carcinoma of whom 368 were males and 52 females. The figures detailed below under 'prognosis' show that the only reasonable chance for a patient with bronchogenic carcinoma to survive 5 years or more is to undergo surgical extirpation of the growth by pulmonary resection. It is important to accept that most undiagnosed unilateral pulmonary masses, abscesses, atelectases or infiltrations are most likely to be due to bronchogenic carcinoma (Fig. 2). Consequently it is far safer to advise, after full and expeditious investigations, exploratory thoracotomy for such cases, than to countenance a policy of diligent observation. Once surgical intervention is accepted the operative risks and post-operative morbidity can be appreciably lessened by careful attention to the patient's general condition. Intensive physiotherapy is mandatory, and so are adequate vitamin and protein intake, blood transfusion if even mild secondary anaemia is present, and quinidine in the older age-groups. Intensive controlled chemotherapy to lessen bronchial and pulmonary secretions and to minimize

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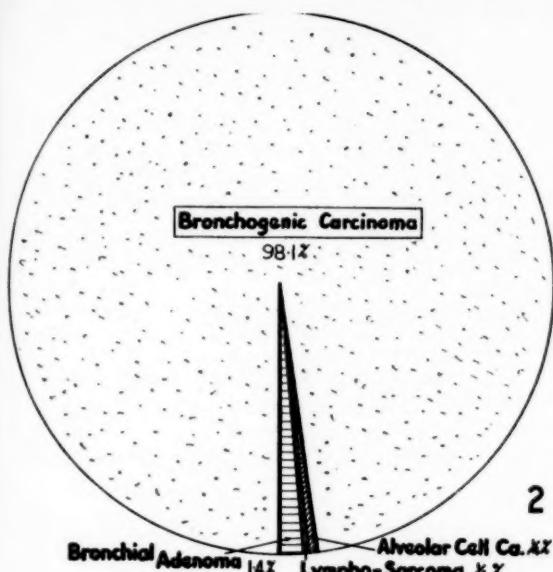


Fig. 2. Primary pulmonary malignancy: 429 cases

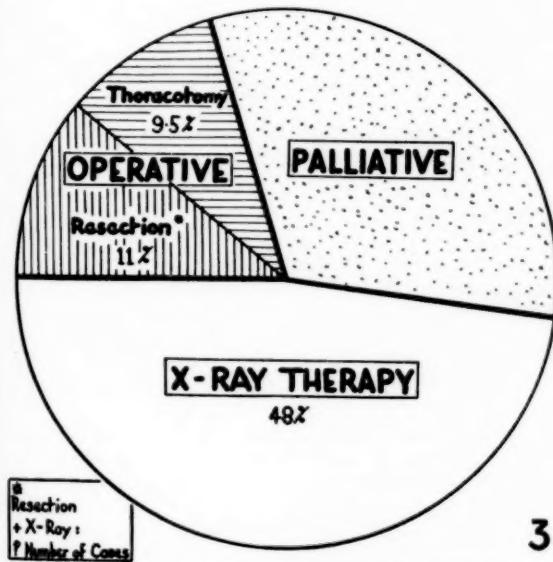


Fig. 3. Therapy in 420 cases of bronchogenic carcinoma

post-operative wound, pleural and bronchial infection will do much to reduce the surgical risks.

#### Contra-indications to Surgery

1. Poor general condition is much more important than age. A young man in poor condition would not be accepted for resection whereas an older man in good shape would be assessed as a good risk.

2. Poor respiratory function—poor chest-wall expansion, emphysema, bronchospasm and bronchitis.

3. Severe cardiac disability (but a preceding coronary is no bar provided function is satisfactory).

4. Presence of extrathoracic metastases.

5. Pleural effusion if haemorrhagic, containing malignant cells or due to pleural secondaries.

6. Extension of growth outside the confines of the lung makes resection often impossible or at best only palliative. Thus hilar growths with involvement of the mediastinal structures, recurrent or phrenic nerve paralysis, chest-wall extension or tumours at the apex are usually excluded from surgery. This also applies to extensive involvement of the posterior mediastinal lymph nodes as shown by indentation on the barium swallow.

7. Bronchoscopic evidence of spread to the tracheal wall or paratracheal glands, or of carinal fixity.

#### Factors favouring surgical intervention

1. Type of growth—squamous-cell carcinoma and adeno-carcinoma are favourable, small-cell carcinoma unfavourable.

2. Asymptomatic 'coin' lesions accidentally discovered on mass radiography are likely to be resectable.

3. A large mass of long duration is more likely to be resectable than a small opacity with a history of recent symptoms.

4. Growths in the parenchyma of the lung.

#### Contra-indications to resection at thoracotomy

These are relative. Resection is considered curative when the lesion is confined to the lung, when the glands are not macroscopically involved, and when the growth is known not to be a small-cell type. When the growth has transgressed the lung, resection is considered to be palliative and is justified in an attempt to relieve the patient of the continued effects of haemorrhage and of suppuration.

#### Pulmonary Resection

The accepted operation is a block-dissection pneumonectomy with removal of the lung and regional mediastinal glands *en masse*. The first successful pneumonectomy was that reported upon by Ewarts Graham<sup>1</sup> in 1933. An intravenous drip is set up on the ipsilateral forearm and the standard thoracotomy incision, either with resection of a rib or an intercostal incision, is employed. As it has been suggested that haemogenous spread of metastases is encouraged by manipulation of the tumour mass the pulmonary veins are ligated and divided first. The pulmonary artery is next secured. The glands, mediastinal structures and pleura are then dissected with the bronchus to the carina. There are many individual techniques for dividing and closing the bronchus. We prefer using interrupted atraumatic braided wire sutures. The bronchial stump is then pleuralized and buried in the mediastinum. Penicillin and streptomycin (1 mega-unit each) is left in the pleural cavity and the incision carefully closed in layers. Bronchoscopic aspiration of the tracheo-bronchial tree is usually employed to remove any residual secretions. These often lie in the trachea at the site of the cuff of the

endotracheal tube. The pressure in the pneumonectomy space is then taken with a manometer and adjusted by aspiration to the mean negative side. Usually 500—1,000 c.c. of blood are given during this procedure—care being taken not to overload the diminished pulmonary circulation.

Post-operative care is directed to the maintenance of adequate oxygenation by a B.L.B. mask and to ensuring that bronchial secretions are readily voided by the relief of pain, Alevaire inhalations, alcohol (by mouth and intravenously) and by the services of a skilled physiotherapist.

Post-operative X-rays are essential to assess the amount of fluid in the space. Air above the fluid is removed when necessary to maintain a central mediastinum. Patients are sat out of bed within a day or so of operation. Antibiotics and vitamins are given for 14 days. On discharge we now advocate a course of deep X-ray therapy to the mediastinum. We do not favour a thoracoplasty to obliterate the space which initially fills up with blood and serum and is ultimately converted into a firm fibrous intrapleural mass.

#### THERAPY IN 420 CASES OF BRONCHIOGENIC CARCINOMA

	Males (368)		Females (52)		Total	Percentage
	Hospital	Private	Hospital	Private		
All cases ..	197	171	34	18	420	100
Radiotherapy ..	111	69	11	10	201	48
Thoracotomy ..	14	20	3	3	40	9.5
Resection ..	20	21	5	1	47	11
Resection mortality *	0	4	1	0	5	1
Thoracotomy mortality	0	1	0	0	1	0.25

\* In the last 31 resections there has only been 1 death (3.2% operative mortality).

#### Prognosis

We have records of 105 cases of bronchogenic carcinoma seen more than 5 years ago with 3 survivors in this group (all 3 following resection), viz. a male of 44 with a squamous carcinoma, a female of 59 with small-cell carcinoma and a female of 63 with squamous carcinoma.

#### PROGNOSIS OF 36 RESECTION SURVIVORS Position in December 1954

Time since operation		Died (cases)	Alive (cases)
1- 6 months	..	..	7
7-12 months	..	..	6
13-18 months	..	..	2
19-24 months	..	..	4
2- 3 years	..	..	2
3- 5 years	..	..	0
5 years and over	..	..	3

Out of 36 resection patients surviving operation 16 lived longer than a year, 7 longer than 2 years and 3 longer than 5 years. (Of those given only X-ray therapy only 2 were known to be alive after a year.)

The prognosis according to other authors is reflected in the following table.

Author	Total Cases	Explora-	Resec-	Opera-	5-year
		tion	tion	Mor-	Survival
Tudor-Edwardes, A. (1946) <sup>2</sup>	1,016	173	70	17%	27%
Ochsner, A. (1954) <sup>3</sup>	1,365	442	442	19%	36.0%
Kirklin, J. W. et al. (1955) <sup>4</sup>	767	369	184	37%	
Holme-Sellors, T. (1955) <sup>5</sup>	689		446	18%	21.0%
Price Thomas, C. (1955) <sup>6</sup>			272		25.5%
Adler, D. I. (1955)	420	87	47	10.5%	27%

Most authors agree with Kirklin, who states that cell type is of great prognostic importance—worst in small-cell carcinoma (9% 5-year survival) and best in squamous-cell carcinoma and adeno-carcinoma, with large-cell carcinoma intermediate in outlook.

#### A. 2-4. OTHER PRIMARY PULMONARY MALIGNANCIES

2. *Bronchial Adenoma.* These tumours are usually described as benign but they are included in this review because a small percentage have been described with distant haematogenous visceral secondaries. They differ from bronchogenic carcinoma in that they occur much more commonly in women, affect a much younger age-group and run a chronic clinical course characterized by frequent haemoptysis and symptoms from bronchial obstruction with distal pulmonary or pleural infection. As none of our 6 cases treated by resection have shown either clinical or histological evidence of malignancy they are not detailed in this paper.

3. *Alveolar-Cell Carcinoma.* This rare type of pulmonary malignancy (also termed pulmonary adenomatosis) can only be accepted with certainty as primary by autopsy, when other primary growths causing pulmonary secondaries can be excluded. This confirmation is lacking in our one male patient aged 69 who underwent a left lower lobectomy in March 1954 and in whom the histology was reported upon as being typical of alveolar-cell carcinoma (confirmed by the Army Institute of Pathology in Washington). He is alive and well 16 months after resection, which was followed by a course of X-ray therapy to the mediastinum.

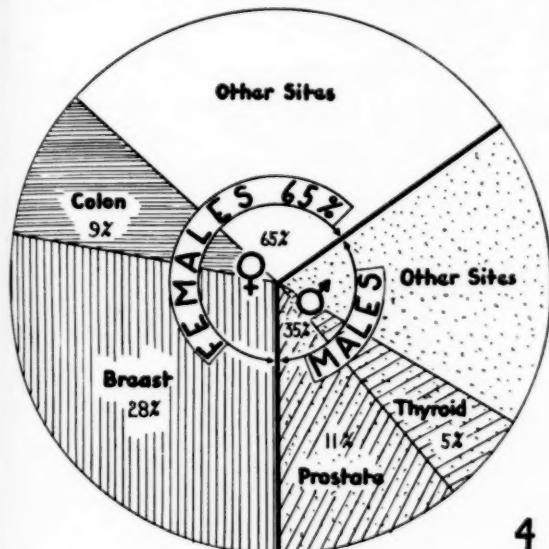
4. *Lymphosarcoma.* We have had one example of this rare tumour in a male aged 29. Almost the whole lung was occupied by a firm fibrous white mass with no evidence of glandular metastases and no pleural involvement. The histological diagnosis in this case was confirmed by Dr. McDonald of the Mayo Clinic, where such cases have been reported.

5. *Haemangiopericytoma.* An example of this rare tumour was seen in July 1955; it is included for interest. A female patient with a coronary thrombosis was admitted to the General Hospital under Dr. M. M. Suzman. Straight X-rays of the chest showed a well-circumscribed homogeneous opacity in the apex of the right lower lobe. Bronchoscopic examination was negative. She died a few weeks later from a further coronary attack; autopsy showed a well-localized

primary mass in the right lower lobe, which proved histologically to be haemangeio-endotheliocarcinoma.

#### B. SECONDARY PULMONARY METASTASES

The following figures are, of course, no index of the origin or incidence of pulmonary secondaries or pleural metastases, since only those cases where the diagnosis was in doubt or where a thoracic surgical opinion was



4

Fig. 4. Secondary pulmonary malignancy: 54 cases

sought are included. We have records of 54 such cases, of which 19 were in males and 35 in females. The prostate in the former and the breast in the latter were the commonest primary sites:

Females	Cases	Males	Cases
Breast	15	Prostate	6
Colon	5	Thyroid	3
Ovary	3	Sarcoma	2
Stomach	2	Melanoma	2
Melanomata	2	Colon	1
Cervix	2	Pancreas	1
Uterus	1	Stomach	1
Sarcoma	1	Adrenal	1
Thyroid	1	Parotid	1
Reticulosis	1	Lymphosarcoma	1
Liver	1		
Gall-bladder	1		
	35		19

Two of these cases were resected. A left lower lobectomy was performed in a female aged 50, 7 months after resection for a primary carcinoma of the colon. In the second case a right upper lobectomy was performed in male aged 54 for what proved at laparotomy 10 months later to be a secondary from a primary adrenal tumour.

#### II. PLEURAL MALIGNANCY

##### A. Primary

1. *Pleural endothelioma.* Many authorities doubt the existence of this condition. One case (even at autopsy) was thought to be due to pleural endothelioma but sections showed that there was a primary adenocarcinoma of the prostate with pleural secondaries. We

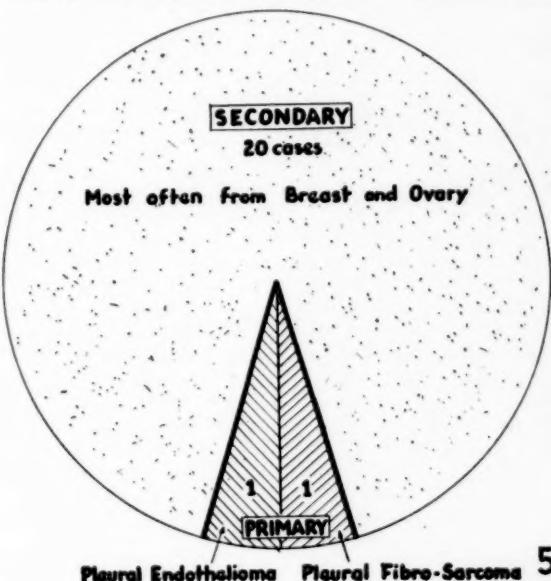


Fig. 5. Pleural malignancy: 22 cases

have seen one case in which autopsy and sections show the histological features of what is described pathologically as pleural endotheliomatosis. This was in a little boy aged 2 years who had a persistent right pleural effusion.

2. *Fibrosarcoma.* The only example of this tumour was seen in 1955, but it is included in this series. These tumours almost invariably arise from the visceral pleura. Our patient, a male of 54, was known to have a small shadow at his right hilum on radiological examination in 1948. When first seen in 1955 he had an orange-shaped homogeneous well-defined mass lying in the right oblique fissure. A pre-operative diagnosis of fibroma of the visceral pleura was made but at thoracotomy malignant change was suspected and middle and lower lobectomy with removal of the tumour *en masse* was fortunately performed in view of the subsequent histological diagnosis of fibrosarcoma.

##### B. Secondary

We have had 20 cases of pleural effusion without demonstrable secondaries in the lung parenchyma on radiological examination. The most frequent primary sites have been carcinoma of the breast and ovary. We have seen several excellent immediate results from aspiration and the intrapleural injection of radio-active gold.

## III. CARCINOMA OF THE OESOPHAGUS

This most distressing disease is by no means infrequent, as shown in a paper to be delivered at a sectional meeting at this Congress by my colleague, Mr. Denis Fuller,<sup>7</sup> who has analysed 80 cases in Johannesburg between the years 1949 and 1954.

Although anatomically it might appear to be impossible to eradicate the primary oesophageal growth and the related lymphatic structures in a block dissection, the results of surgical extirpation are nevertheless most encouraging. Firstly the patient is able to swallow soon after resection of his growth, a matter of some psychological importance. Secondly the long-term survival rate is altogether better after surgery than after radiotherapy alone. Thirdly death occurs from distant metastases rather than from local complications due to infiltration of the trachea, pleura or posterior mediastinum by the growth. In brief surgery aims at removal of the growth and the regional lymphatics, and the establishment of a normal swallowing mechanism. For carcinoma of the distal third of the oesophagus and cardia a left thoraco-abdominal approach is used to extirpate the growth and to perform either an oesophago-gastrostomy or oesophago-jejunostomy. For growths at the level of the aortic arch or higher, where mobilization may prove difficult, there is some advantage in first freeing the stomach by an abdominal approach and then removing the oesophagus and performing the anastomosis through a right thoracotomy incision (on the right the oesophagus is sub-pleural throughout and is readily accessible).

The operative mortality for these cases is about 15%. Mr. Fuller<sup>7</sup> performed an oesophago-gastrectomy in 13 consecutive cases with only one death, i.e. an operative mortality of 7.7%. Sweet reports a 5-year survival rate of 17% for the lower end of the oesophagus and 34% at the cardia.

## IV. MEDIASTINAL MALIGNANCY

## A. Primary

The presence of a localized opacity seen radiologically in the mediastinum calls for urgent thoracotomy (a) provided that generalized reticulosclerosis and bronchogenic carcinoma can be excluded, and (b) provided that, if the patient is in poor general condition this is due to compression by the tumour mass and not to metastases.

1. THYMIC ORIGIN. In our experience most primary growths in the anterior mediastinum are derived from the thymus. An exact pathological classification of thymic malignancy is difficult—even Sir Geoffrey Keynes hesitates to give one.

(a) *Lympho-epithelioma* of the thymus has been the commonest in our series. It is worth recording that many thymic tumours occur in persons not suffering from myasthenia gravis, and that only about 15% of myasthenics harbour a thymic tumour.

The prognosis in the cases of myasthenia is poor according to Keynes<sup>8</sup> unless they have had pre-operative X-ray therapy. We have operated upon two such

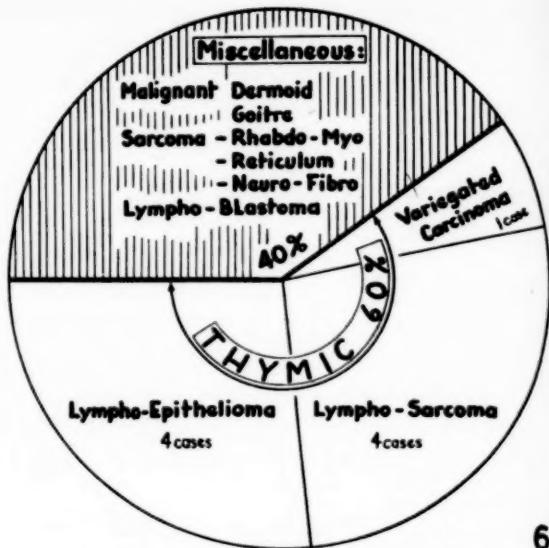


Fig. 6. Primary mediastinal malignancy: 15 cases

cases—both young women under the age of 25. One—a case of Dr. M. M. Suzman's—was dramatically improved for 9 months and died of ? pneumonia. The other—a case of the late Dr. J. B. Baynash—died post-operatively, and autopsy showed multiple haemato-gogenous pulmonary and hepatic secondaries.

We have records of 4 malignant thymic lympho-epitheliomas unassociated with myasthenia. One was found in a female of 27 who was admitted with an effusion in her knee-joint. This was thought to be tuberculous, but a routine chest film showed a large irregular mass lying in the right anterior costo-phrenic sinus. This was removed at thoracotomy, the patient surviving for 7 months; autopsy was refused. The second case was in a male aged 33, who had complained for 3 weeks of pain in the left chest and a transient minor haemoptysis. Thoracotomy revealed a thymic tumour with widespread invasion of pericardium and left upper lobe. The growth was successfully removed, but no follow-up has been possible. The third case, referred by Dr. I. Freed, occurred in a male of 34, who was found to be hopelessly inoperable at thoracotomy. This patient is alive and well 26 months after deep X-ray therapy by Dr. M. Weinbren. The fourth case was inoperable and died several weeks after median sternotomy.

(b) *Variegated carcinoma* of the thymus was first described by Lowenhaupt<sup>9</sup> in 1948. We have seen this rare tumour once in a recent case referred to us from Prof. G. A. Elliot's wards at the Johannesburg General Hospital by Dr. M. Posel. The tumour occupied most of the right chest and the anterior mediastinum and passed well over to the left of the mid-line. It was successfully removed through a right antero-lateral incision with transverse section of the sternum and ligation of the internal mammary vessels on both sides.

Deep therapy was given both before and after operation, and radio-active gold was injected intrapleurally 10 days after operation, but skin secondaries occurred after 5 months.

(c) *Lymphosarcoma* of the thymus has been seen on 4 occasions—3 in males and 1 in a female. One of these cases lived for 11 years after the initial diagnosis and after repeated courses of X-ray therapy. These cases are very radio-sensitive.

2. MISCELLANEOUS MEDIASTINAL MALIGNANCY. (a) *Malignant Dermoid*. According to Rusby<sup>10</sup> 13.8% of mediastinal dermoids have been reported upon as being malignant. We have had one such case in a woman of 37. Her tumour, thought to be benign, was removed at thoracotomy but malignancy was found on histological section. A year later a secondary nodule containing intestinal mucosa was removed from the skin incision.

(b-f) One case each of carcinoma of an aberrant intrathoracic goitre, of rhabdomyosarcoma, of reticulum-cell sarcoma, of neurofibrosarcoma and of giant follicular lymphoblastoma has occurred. The exact pathology was only diagnosed by histological examination following autopsy.

#### B. Secondary Mediastinal Malignancy

1. *Generalized reticulosis*. We have seen 6 examples of this in Hodgkin's disease. One case, in a woman of 42, presented with a swelling of the right 2nd costal cartilage. She narrowly avoided thoracotomy by developing a gland in the neck on the day of the projected mediastinotomy!

One young female presented with the symptoms of tracheobronchial compression and calcified tuberculous foci in her lungs. Widespread body pains, however, were shown to be due to metastases and the hilar invasion was due to reticulososis.

2. *Secondary mediastinal glandular carcinoma*. The commonest primary is bronchogenic carcinoma, and less commonly carcinoma of the breast and oesophagus. Any carcinoma may, however, metastasize in the mediastinum.

#### V. CHEST WALL

##### A. Primary

1. *Ewing's sarcoma* of rib has been seen in a child of 4 and in a girl of 15. Both tumours responded initially to deep therapy, but the patients eventually died.

2. *Chondrosarcoma* of rib. A case of this condition survived 18 years after wide excision of the chest wall by Mr. A. Radford of Durban. The growth recurred several years before the patient's death, at which stage he also had pulmonary metastases.

3. *Fibrosarcoma* of rib. This occurred in a woman of 35, who remains well and free from recurrence 30 months after removal.

4. *Fibrosarcoma* of diaphragm. This rare tumour occurred once in an infant 2 years old. The child died 6 months after exploratory thoracotomy.

##### B. Secondary

1. (a) Carcinoma of the bronchus with invasion of the chest wall has presented as a large mass causing severe pain from involvement of the intercostal nerves.

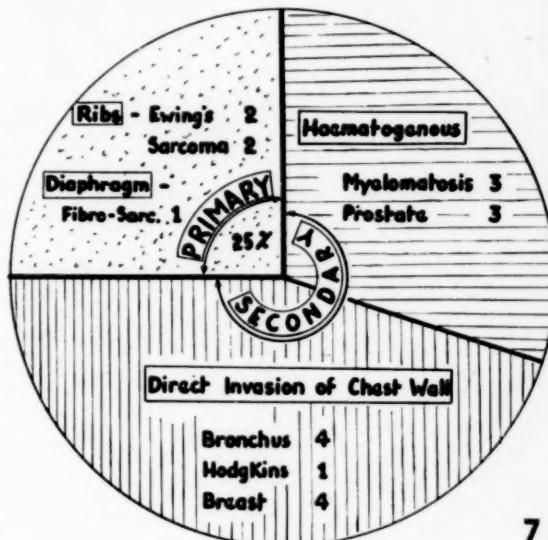


Fig. 7. Chest-wall malignancy : 21 cases.  
(For SARCOMA 2 read SARCOMA 3).

For these cases injection of 1 in 20 phenol into the subarachnoid space has been of some assistance.

2. (b) Secondaries in ribs from carcinoma of the prostate have been suspected by their dense sclerosis and confirmed by rectal examination and a high level of serum acid phosphatase.

#### CONCLUSION

Of 636 cases of intrathoracic malignancy, 420 (67%) were cases of primary bronchogenic carcinoma, 80 were derived from the oesophagus, and the balance were of heterogeneous origin.

A plea is made for early surgical intervention, since 5-year cure is only seen after surgery.

I should like to thank Dr. K. Mills, Medical Superintendent, Johannesburg General Hospital, for permission to review the hospital cases, Professor W. Underwood of the Department of Surgery, University of the Witwatersrand, for the thoracic surgical facilities, and Mr. L. Fatti for allowing me to include some of his hospital cases.

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## MAKERERE COLLEGE MEDICAL SCHOOL, KAMPALA, UGANDA

The following is abstracted from a letter of Christmas greeting which Dr. G. W. Gale, Professor of Preventive Medicine at Makerere College Medical School, Kampala, Uganda, and formerly Secretary for Public Health, Union of South Africa and Dean of the Faculty of Medicine, University of Natal, has sent to his friends in South Africa:

.... We arrived in Kampala on 8 May 1955, having travelled by sea from Durban to Mombasa, thence by car—via Nairobi, Eldoret and Jinja. At Jinja we crossed the Nile, as it leaves Victoria Nyanza, by the lofty Owen Falls Dam, from which electricity will be distributed to a vast area. Kampala is another 50 miles and for years was the terminus of the railway; but they are now extending westwards for 250 miles to the Kilembe copper and nickel mines on the slopes of the Ruwenzori Range—the 'Mountains of the Moon'. The whole of Uganda is developing very rapidly—industrially, commercially, agriculturally, educationally and politically—and Kampala is the hub of the country ....

Makerere is the University College of East Africa, and draws students from Uganda, Kenya, Zanzibar, Tanganyika and even Rhodesia. There are no racial bars, but European students are rare and Indians only a small minority. All students reside at the College, which has extensive grounds on one of the 'seven hills' of Kampala. Nearly £2 million has been spent on buildings and equipment and another million will be spent over the next 5 years. It is anticipated that the enrolment will increase from 540 (this year) to nearly 2,000 by 1961. Even so, Makerere will scarcely keep pace with the demands of the rapidly expanding economy of these parts of Africa. There is a basic 2-year course for all, after which students diverge to a further 2 years for B.A. and B.Sc. (University of London external examinations), or the longer

professional courses for the College diplomas in education, medicine, agriculture, veterinary science and arts and crafts. The course in medicine is 5 years (after the basic 2) and is of full professional standard. Clinical teaching is at the Mulago Hospital immediately adjacent, 650 beds. It is about to be replaced by a new 800-bed hospital to cost a million.

.... The eagerness and responsiveness of the students makes them a pleasure to teach. English is the medium—even of inter-communication between many of the students, who come from a wide diversity of language-groups. The University students wear sleeveless red gowns, which give a gay colouring to the campus, dining halls and official functions. There are only 50 women, for East Africa has been a long way behind in the matter of female education; but is now catching up!

Its geographical situation .... makes Makerere the scene of frequent university-level inter-territorial conferences and occasional international conferences on all sorts of topics; and there is also a steady flow of individual visitors from university and research institutions from other parts of the world .... The climate has surprised us by its coolness—about the same as warm winter days in Durban—but it is monotonous, as there are no seasons and the days do not vary in length. Rain is frequent—in storms and heavy showers, with plenty of sunshine between—so that the vegetation is lush and always green and there are many fine indigenous trees. 'The Lake' is only 5 miles away; and 21 miles distant (by a tarmac road) is Entebbe which, with its Botanical Gardens and extensive public lawns beside the Lake, is a most attractive spot.

.... But, of course, we do miss our beloved South Africa very much—the land itself, its turbulent politics and, most of all, those dear to us through kinship and the long years of friendship.

## SOUTH AFRICAN SOCIETY FOR INDUSTRIAL HEALTH

The Cape Town sub-group met at the New Somerset Hospital, Cape Town, on 16 November 1955, when addresses were given by Mr. A. Singer, M.Ch.Orth. (L'pool), and Mr. N. Rosenzweig, F.R.C.S. (Edin.), M.Ch.Orth. (L'pool), on the treatment and rehabilitation of orthopaedic patients. The meeting was arranged by Dr. L. Blumberg.

## INJURIES OF THE LOWER LIMBS

Mr. A. Singer dealt with injuries of the lower limbs. He classified injuries as:

1. *Minor*—Those that can be dealt with adequately on the spot by the factory doctor and sent back to work.
2. *Major*—Those that must be transferred to hospital without delay. For successful rehabilitation this must be accomplished with speed and safety.

*First Aid Treatment.* The patient should be splinted where he lies and bleeding controlled by digital pressure at classical pressure-points, application of artery forceps or even digital pressure on the wound in extreme emergency—never by tourniquet. 'More limbs have been lost by leaving tourniquets on too long than have been saved by them'.

Warmth must be applied to counteract shock, and generous use of morphine will help to allay fear and pain, which are contributory factors to shock.

The ideal means of transport is by a 'sorbo' rubber bed, placed on a specially-sprung ambulance stretcher. By acting as a shock-absorber, this method reduces pain to a minimum and so contributes to the lessening of shock.

Where indicated, surgical treatment should commence without delay, especially in severe injuries of the elbow and ankle, because the rapid onset of reactionary oedema makes closed manipulation difficult. When left too long oedema blisters make open operation extremely hazardous.

The guiding principle of fracture treatment is the three *Rs*: (1) Reduction, (2) Retention, and (3) Rehabilitation (*a*) of the injured part and (*b*) of the patient.

In treating lower limbs, good alignment is the main objective, because mal-alignment is the major cause of osteo-arthritis in the associated joints.

Oedema is minimized by adequate and correct splinting and early orthopaedic care.

Mr. Singer showed X-rays demonstrating the good results of early treatment, and the problems set by delay.

## INJURIES OF THE HAND

Mr. N. Rosenzweig opened his address by describing the hand as the most important part of the body, especially from the economic point of view. Of 2 million disabling injuries occurring annually in the USA no less than 75% affect the hand. Thirty per cent of accident and occupational disease benefits in England in 1949 were paid out for hand injuries.

Stiffness of even one finger from a minor injury can be more disabling than a fractured limb. Compound fractures of the phalanges can present greater difficulties in management from the economic standpoint than compound fractured femurs.

In *first-aid treatment* the tourniquet was again condemned. A sterile gauze dressing, pressure and immobilization of the fingers in the position of function (i.e., in the semi-flexed position) was necessary. Each finger should be individually splinted or bandaged, for the digits are not meant to lie parallel in the position of rest, and the tip should point towards the scaphoid tubercle; there are few exceptions. The thumb should be immobilized in the position of opposition and not widely abducted.

The *functional position of the wrist* is automatically obtained by making a strong closed fist. In treating a fractured carpal, the interphalangeal joint of the thumb should be included in the cast. An easy way to construct the plaster cast is as follows: Make the patient grip a narrow cylinder. Then apply a plaster slab from the knuckle head to just below the elbow along the dorsum. Apply a narrower slab from the base of the thumb nail to midway up the forearm meeting the first slab in a V. When the plaster is moulded and set the patient opens his fingers and completion of

the cast is simple, by application of a p.o.p. bandage. It should be moulded well into the palm and not extended beyond the transverse mid-palmar crease.

In *mild strains of the digital joints*, where the ligaments are not completely torn, unless the joints are supported and active exercises performed, pain, swelling and stiffness may persist for some while. Where a ligament is torn completely, with or without an associated fracture, more rigid immobilization is required and despite adequate treatment, pain, swelling and stiffness require reassurance, for it may persist for many months.

In the *after-treatment of dislocations* it should be remembered that a complete tear of the ligaments precedes a dislocation and therefore immobilization is required. Specific fractures, dislocations and tendon ruptures were briefly discussed. Open injuries were only lightly surveyed.

There are 3 degrees of closed joint-injuries of the digits:

1. Torn fibres or attachments of the ligaments.
2. Detached ligament with or without a flake of bone (one degree off a frank dislocation).
3. Dislocation.

Potential stiffness in No. 1 can be overcome by elastoplast support and active exercise.

No. 2 presents the features of a spontaneously reduced dislocation and should be treated as such. Immobilization followed by active exercise and avoiding passive stretching should be adopted, although, in spite of treatment, pain and swelling may persist for 3-6 months.

In No. 3 adequate immobilization is necessary to allow the torn ligaments to heal. Anything less leads to recurrent dislocations, when reconstruction of the ligaments might have to be considered.

*Severed flexor tendons* should be repaired as a primary measure. Instead, healed skin and subsidence of inflammation should be achieved as soon as possible and the patient encouraged to co-

operate in passive movements. Unless a full range of these movements are obtained, reconstructive surgery of tendons is bound to be a failure.

Should *amputation of the whole of a terminal phalange* be necessary the flap should be reflected back, so that the nail bed is exposed and radically excised. A simple skin-graft is obtained by cleansing the forearm and raising a blister by a subcuticular injection of procaine and adrenaline. Several hypodermic needles are then inserted transversely through the bleb, and the thin layer of skin superficial to the needles is shaved off and applied to the denuded area with a pressure dressing.

Answering a question Mr. Singer stated that the self-respect of the patient was best stimulated by returning him to his own work as soon as possible. Adequate early treatment was the best means of achieving this.

Dr. M. P. Freedman thought that, if employers knew that the W.C.A. Commissioner continues to pay 66% of the basic wage up to £40 p.m. for an indefinite period while the injured worker is only partially employed, they might be less reluctant to re-employ him. Trade Union regulations were mentioned as an obstacle to the employment of a skilled worker in any job other than his own.

Dr. L. Blumberg thanked the lecturers for a most instructive evening, from which he and everybody present had learnt a great deal. He appealed to the doctors present to join the Association for Industrial Health in order to make it functionally useful, both to the worker and to the industrialist. He hoped that next year each speaker could spare a full evening for discussing his subject with a larger audience.

Dr. Freedman announced that a meeting of the sub-group of the South African Society for Industrial Health would be held on 25 January, when the aims and objects of the Association would be explained and new members invited to join the group.

## OFFICIAL ANNOUNCEMENTS :

### LIFE INSURANCE EXAMINATION FEES

Members are advised that as from 1 December 1955 the fees for life insurance examinations will be increased to £2 2s. 0d. per examination.

Members are reminded that this fee is for a full examination, and supplementary reports containing information which should have been included in the original report will not be subject to an additional fee. Furthermore, additional examinations or special reports which are beyond the scope of the ordinary Report Form are not subject to an additional fee unless requested and authorized by the life insurance office concerned.

### DONATIONS TAX

Members are advised that the Honourable the Minister of Finance has, in terms of Section 54 quat. (1) (i) and (j) of the Income Tax Act, exempted from the donations tax all donations made to or by the Medical Association of South Africa Benevolent Fund.

A. H. Tonkin  
Secretary

Medical House  
Cape Town  
1 December 1955

### MEDICAL AID SOCIETIES ADDED TO THE LIST

The following Medical Aid Societies were approved by Federal Council at its meeting held in Pretoria on 13-15 October 1955:

Pongola Sugar Milling Company Limited Medical Benefit Fund, 301 Smith Street, Durban.

Springbok Medical Aid Society, P.O. Box 7614, Johannesburg.

Approval was also granted to the following Benefit Society to operate on the Tariff of Fees for Approved Medical Aid Societies for Specialist Services (Second Schedule in Tariff Book).

Springs Mines Benefit Society, P.O. Box 54, Springs, Transvaal.

### AMPTELIKE AANKONDIGINGS

#### GELDE VIR ONDERSOEKE VIR LEWENSGESEKERING

Lede word in kennis gestel dat die gelde vir ondersoeke vir lewensversekering met ingang van 1 Desember 1955 tot £2 2s. 0d. per ondersoek verhoog word.

Lede word daaraan herinner dat hierdie bedrag 'n volledige ondersoek dek. Aanvullende rapporte met inligting wat eintlik tot die oorspronklike verslag behoort, sal nie vir bykomstige betaling in aanmerking kom nie. Daarbenewens kom addisionele ondersoeke van spesiale rapporte wat buite die bestek van die gewone verslagvorm val nie vir addisionele gelde in aanmerking nie, tensy aangevra en gemagtig deur die betrokke lewensversekeringsmaatskappy.

### DONASIEBELASTING

Lede word in kennis gestel dat sy Ed. die Minister van Finansies, ingevolge Seksie 54 quat. (1) (i) en (j) van die Wet op Inkomstebelasting, alle donasies aan of deur die Liefdadigheidsfonds van die Mediese Vereniging van Suid-Afrika van donasiebelasting vrygestel het.

Mediese Huis  
Kaapstad  
1 Desember 1955

A. H. Tonkin  
Sekretaris

### MEDIESE HULPVERENIGINGS TOT DIE LYS GEVOEG

Op sy vergadering van 13-15 Oktober 1955 te Pretoria gehou het die Federale Raad onderstaande nuwe Mediese Hulpvereniging goedgekeur:

Pongola Sugar Milling Company Limited Medical Benefit Fund, Smithstraat 301, Durban.

Springbok Medical Aid Society, Posbus 7614, Johannesburg.

Goedkeuring was ook gegeen aan die volgende Siekefondse om gebruik te maak van Spesialistdienste teen die tarief vir Mediese Hulpverenigings (Tweede Lys in die tarieweboek).

Springs Mines Benefit Society, Posbus 54, Springs, Transvaal.

## MEDICAL AID SOCIETIES REMOVED FROM THE LIST

Members of the Association are notified that the following name is to be removed from the List of Approved Medical Aid Societies with effect from 1 January 1956:

National Medical Aid Society of South Africa, P.O. Box 4028, Cape Town.

Medical House  
Cape Town  
9 December 1955

L. M. Marchand  
Associate Secretary

## MEDIËSE HULPVERENIGINGS VAN DIE LYS GESKRAP

Lede van die Vereniging word in kennis gestel dat die naam van die volgende Hulpvereniging van die lys van goedgekeurde Mediese Hulpverenigings geskrap moet word, met ingang 1 Januarie 1956.

National Medical Aid Society of South Africa, Postbus 4028, Kaapstad.

Mediese Huis  
Kaapstad  
9 Desember 1955

L. M. Marchand  
Medesekretaris

## IN MEMORIAM

THE LATE MR. MARCUS COLE ROUS \*

*Mr. P. J. M. Retief, of Cape Town, writes:* When Dr. Cole Rous died I, together with many others, lost a close friend and the medical profession lost a brilliant and respected colleague. His end was so sudden that many of his closest associates never even heard of his illness and the first news they had was of his death. In memory of our friendship and my deep sense of gratitude to him, I would like to recall a few of the many pleasant memories I have of him.

I had the privilege of first learning to know this remarkable man and outstanding surgeon as a student when he taught us surgical pathology. How he made those cold grim bottled specimens live and talk! How exhilarated we all became by his enthusiastic and lucid exposition of each problem!

Then later at ward rounds I heard again the familiar dynamic and logical approach to clinical problems and came away from each encounter richer in knowledge and with a bursting desire to emulate if I could this vital method of mastering medical knowledge. From his housemen he was satisfied with nothing less than perfection, and what he gave himself he expected from his assistants. He was always ready to teach and he taught superbly. Students coached by him very seldom failed and often did brilliantly. He not only taught them medicine and surgery, but inspired them with confidence and showed them how to present the knowledge they had in a manner most acceptable to the examiner.

I would like very briefly to recount a little about Dr. Cole Rous' earlier life. He grew up on a sheep farm at Middelburg, Cape, and went to school at S.A.C.S., Cape Town. He graduated in Medicine from the Cape Town University in 1927, where he distinguished himself in his clinical years. After housemanships with Professors Saint and Falconer he took the English F.R.C.S.

\* An In Memoriam notice concerning Mr. Cole Rous was published in the *Journal* of 3 December 1955 (29, 1154).

and returned to Cape Town, where he commenced his surgical practice as assistant to Professor Saint. In a short time he became one of Cape Town's leading consultants. He took an active part in teaching at the University and from early on was an enthusiastic member of the Cape Western Branch of the Medical Association of South Africa. He enlisted early in the last war, saw service in East Africa, and rose to the rank of Lieutenant-Colonel, S.A.M.C.

It was during the post-war period that his continued exertions finally took toll of his health; he developed a coronary thrombosis at the early age of 43 years. This illness had a sobering effect upon him. He realized he had been burning the candle at both ends and he set himself with remarkable fortitude to remodel the tempo of his existence. He cultivated a love for philosophy, gave up watching the clock while operating, and found peaceful recreation by sailing a yacht in the blue waters of Table Bay. So successfully did he curb and re-canalize the restless spirit that bubbled turbulently within him, that he enjoyed 9 years of good health and productive living. During these years he made many friends, remained a master surgeon, and increased his stature in the highest councils of the Medical Association.

Many colleagues will remember Dr. Cole Rous as one ever willing to assist someone in trouble. His logical mind quickly grasped the many facets of legal argument, and his advice and support in such difficulties were invaluable. Many men are intelligent but lack the courage to give the world the benefit of their reflections. Here was a man who did not allow fear to divert him from what he believed to be the right course. He often stood up for the underprivileged and the underdog, for with him colour, caste and creed held no prejudice. His courage enabled him to rise above the everyday difficulties of life and at all times to be cheerful and optimistic. I believe these two characteristics stem from the fact that he never bemoaned his own fate nor did he ever say an unkind word about his neighbour.

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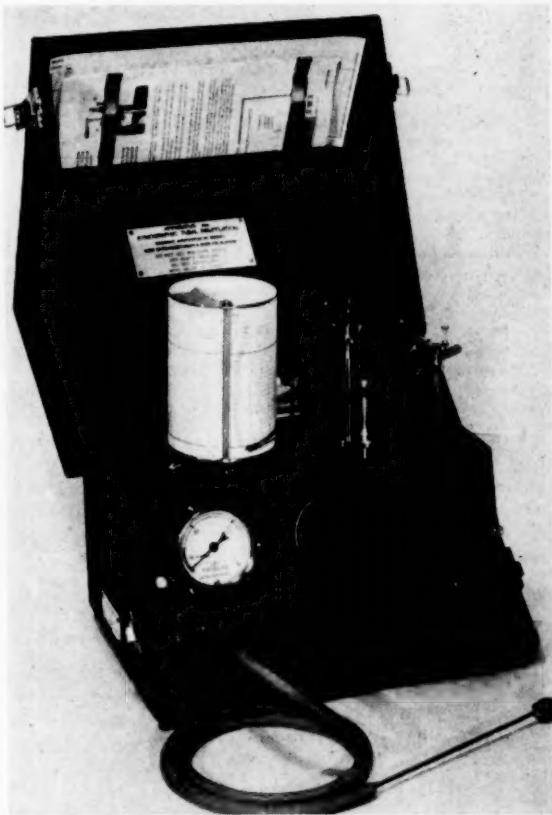
*Winton, F. R. and Bayliss, L. E.* Human physiology. 4th ed. Churchill, 1955.

## NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

### *The New Sharman's Kymographic Tubal Insufflation Apparatus*

The manufacturers, Kelvin and Hughes (Industrial) Ltd., supply the following particulars:

This apparatus, which incorporates the principle introduced by Rubin and modified by Bonnet, has been used for some time by the leading sterility clinics in Great Britain. Recording as it does a graph of insufflation, the equipment has now been produced in an improved and simplified form. The whole control is obtained



by means of a single 4-position flow-control valve instead of the two infinitely variable valves previously fitted. Improved valve design ensures consistent operation over long periods. The CO<sub>2</sub> storage-cylinder capacity is sufficient for a large number of operations without changing.

The use of the intertubal insufflation with carbon dioxide for the determination of tubal patency or non-patency in cases of sterility is now universal. The addition of a kymograph gives definite evidence not only of normal tubal patency, function and non-patency but also of tubal dysfunction and pathology—e.g. spasm and stenosis.

Originally developed by Dr. Sharman of Glasgow, the design is simple and construction robust, whilst performance is accurate and reliable. This particular equipment is in use in every women's hospital in the United Kingdom.

## PASSING EVENTS : IN DIE VERBYGAAN

Mr. S. Scher, F.R.C.S., of Cape Town, has returned from a 3 months' visit overseas.

Dr. C. de V. Bevan and family have returned from London, where

Dr. Bevan obtained the Diploma in Clinical Pathology at Hammersmith Hospital Postgraduate Medical School. He has now taken up an appointment with the South African Institute for Medical Research, Johannesburg.

## BOOK REVIEWS : BOEKRESENSIES

## ORTHOPAEDIC MEDICINE

*Text-Book of Orthopaedic Medicine, Volume I. Diagnosis of Soft Tissue Lesions.* By James Cyriax, M.D., B.Ch. (Cantab.). Pp. 692 + xiv, with 128 Illustrations. 45s. London: Cassel and Company Ltd. 1954.

**Contents:** 1. Medical Fallacies. 2. Traumatic Inflammation. 3. Referred Pain. 4. Nervous and Pressure on Nerves. 5. Non-specific Arthritis. 6. Diagnosis of Soft Tissue Lesions. 7. Head, Neck and Scalp Area. 8. Thoracic Outlet-Jaw. 9. Shoulder—Part I. 10. Shoulder—Part II. 11. Shoulder—Part III. 12. Elbow. 13. Wrist and Hand. 14. Thorax and Abdomen. 15. Lumbar Region—Part I. 16. Lumbar Region—Part II. 17. Lumbar Region—Part III. 18. Lumbar Region—Part IV. 19. Sacro-iliac Joint, Buttock and Hip. 20. Knee. 21. Leg and Ankle. 22. Foot. 23. Anaesthesia and Analgesia. 24. Psychogenic Pain. 25. Physician and Physiotherapist. Index.

Dr. Cyriax has written an interesting book concerning the clinical aspects of most of the soft-tissue complaints met with in orthopaedic and physiotherapy clinics. The emphasis of his approach has been on the clinical rather than the academic aspects of the problem.

As a result, the viewpoint expressed appears to be dogmatic and over-simplified in a number of subjects about which there is contention in current literature. For instance, 'First-Rib Pressure Syndrome' is at present very much under review and revision, and it is a little difficult to accept as final Dr. Cyriax's concept. Similarly, his 'Dermatome Patterns' are different from those of other authorities such as Foerster and Keegan.

However, it is an excellent thing in a clinical field to lay down the law as a starting point. Modification can always be made later.

There is a definite need for a comprehensive work in the field of physical medicine, and I am sure Dr. Cyriax's book will be a good working companion for those employed in this field. This book also offers much food for thought for all orthopaedic surgeons and students interested in the subject.

C.E.L.A.

## CHILD MANAGEMENT FOR PARENTS

*Babies and Young Children. Feeding, Management and Care.* By Ronald S. Illingworth, M.D. (Leeds), F.R.C.P., D.P.H., D.C.H., F.R.P.S. and Cynthia M. Illingworth, M.B., B.S. (Hons.) (Durham), M.R.C.P. (Lond.). Pp. 360 + vii, with Illustrations. 18s. London: J. & A. Churchill Ltd. 1954.

**Contents:** 1. Planning and Preparations for a Child. 2. Some Features of the Newborn Baby and His Care. 3. On Crying in Babies. 4. How will He Grow? 5. Breast Feeding. 6. Artificial Feeding. 7. Weaning. 8. The Premature Baby. 9. How Children Develop. 10. Variations in Development. 11. How can the Child's Development be Helped? 12. Toys and Play. 13. Some Aspects of Child Management. 14. On Love and Security. 15. Some Manifestations of Insecurity. 16. Some Annoying Features of Children. 17. Sex Interest and Masturbation. 18. Discipline. 19. Punishment and its Avoidance. 20. Troublesome Children. 21. Sleep. 22. The Appetite After the Weaning Period. 23. Toilet Training. 24. Miscellaneous Problems. 25. Some Special Problems of Management. 26. The Prevention of Infection. 27. The Prevention of Accidents. 28. The Teeth. 29. The Bowls. 30. Some Common and Important Symptoms. 31. The Treatment of the Ill Child. Epilogue. Some Recommended Reading. Index.

This is a book for lay people written by a medical couple both of whom have paediatric experience as well as having been recently 'through the hoops' as parents of a young family. The result is a book which should be very welcome and of great value to all parents of young families—medical or lay. The physical and psychological aspects of most of the innumerable problem-situations of ordinary family life with infants and small children are considered in detail and common sense is nicely blended in the

solutions offered. Possibly the psychological approach is a little more prominent than is quite necessary, but it is used to present small children to their parents as rational and very astute beings, not as idols to be worshipped or idiots to be whacked. There is plenty of factual information also.

It would pay most general practitioners to have this book on their shelves. It supplies the answer to parents' inquiries as to what book they might buy for guidance. This is certainly such a book, and a good one. And the price is not excessive.

F.J.F.

## AGEING: CIBA COLLOQUIA

*Ciba Foundation Colloquia on Ageing: Volume I General Aspects.* Edited by G. E. W. Wolstenholme, O.B.E., M.A., B.Ch. and Margaret P. Cameron, M.A., A.B.L.S. Pp. 255+xii with 38 illustrations. 30s. London: J. & A. Churchill Ltd. 1955.

**Contents:** 1. Chairman's Opening Remarks. 2. The Definition and Measurement of Senescence. 3. Some Remarks on the Pathological Basis of Ageing. 4. Mental Aspects of Ageing. 5. Effects of Ageing on Respiratory Function in Man. 6. Changes with Age in Diffusion Coefficients of Solutes for Human Tissue Membranes. 7. The Changing Incidence of Certain Vascular Lesions of the Skin with Ageing. 8. Ageing of Elastic Tissue and the Systemic Effects of Elastase. 9. Calcium Metabolism in Old Age as Related to Ageing of the Skeleton. 10. 17-Ketosteroid Excretion in Ageing Subjects. 11. Tissue Transplantation Technique Applied to the Problem of the Ageing of the Organs of Reproduction. 12. Preservation of Tissue *in vitro* for the Study of Ageing. 13. Research Areas in Gerontology Nutrition that are now Neglected. 14. A Fantasy of Ageing and the Bearing of Nutrition upon it. 15. Too Rapid Maturation in Children as a cause of Ageing. 16. Psychological Aspects of Ageing. 17. Adrenocortical Reactivity in Aged Schizophrenic Patients. General Discussion.

This book follows the usual well-known pattern of the Ciba Colloquia. Experts from many countries contribute papers, which are part reviews, part original, and are followed by free-for-all discussions. These discussions are reported verbatim—or nearly so, presumably after some editing by the experienced Wolstenholme and by the speakers themselves. This editing seems a little more serious than in similar American publications, as judged by the absence of those wholly irrelevant asides which, while not contributing much to the scientific aspects of the subject, at least contribute a good deal to our picture of the personality of the participants. In this work one may read of ageing in unicellular organisms, in rotifers, insects, sea-anemones, turtles, trout, pigs, elephants, birds, and all the usual animals as well. One may read of discussions on the wrinkling of the skin, volume of the lungs, calcium absorption, performance of skilled actions, excretion of 17 ketosteroids, glucose tolerance in schizophrenics, importance of heredity, importance of teeth, bronchiectasis in rats, autopsies on centenarians, and so on. Of most particular interest, running right through the book, is the consideration of the importance of nutrition before puberty on longevity. There seems to have been countless experiments and observations going back many years which indicate that overfeeding in the young of many species will lead to over-rapid maturation and a short life, whereas underfeeding will delay maturation and lengthen life. There are many indications that this applies to man—that we should not necessarily congratulate ourselves if our children are taller and heavier than they were 100 years ago.

Much of this book is interesting, but much seems to be very superficial and the quality is variable. The chapter on the skeleton, for instance, was disappointing. McCance's contribution, as usual, was most stimulating—particularly his idea of the possibility of damage to pancreatic islets by overfeeding them rather than by overworking them.

The subject is one of great and growing importance and a perusal of this work will show the reader how little we know of it.

W.P.U.J.

## CORRESPONDENCE : BRIEWERUBRIEK

## LOCKED TWINS

To the Editor: In the *Cape Times* today there is a short article describing a rare case of locked twins in which both babies were born alive. I had a similar case at the Hope Hospital, Salford, England, which was dealt with by a method—albeit unorthodox—which resulted in the birth of two living babies.

A patient aged 28 (para 3, all normal spontaneous deliveries, the last baby weighing 9 lb. 7 oz.) was admitted on 27 December 1952, when 34 weeks pregnant (by her dates), because of premature rupture of the membranes. On 29 December at 11.0 a.m. labour commenced spontaneously, and by 6.30 that evening, i.e. 7½ hours later, she was fully dilated, and the presenting baby, a breech, came down on the perineum. At this stage the patient was prepared as for a breech delivery, placed in the lithotomy position, draped with sterile towels, and catheterized, and local anaesthetic injected into the perineum for an episiotomy, notwithstanding that the perineum was extremely lax. This extreme laxity has a bearing on the treatment that was adopted.

The case proceeded satisfactorily until the delivery of the arms. They were flexed, and the posterior arm was delivered first, but a little difficulty was experienced in bringing down the anterior arm. When the arms were born it was noticed that the neck was acutely extended, and it was evident that the head was above the brim and was being prevented by something from engaging. A vaginal examination soon revealed that the reason was that the head of the second baby was in the pelvis and the head of the baby which was being delivered was above it.

It was difficult to decide what to do in these circumstances. An unsuccessful attempt was made to push the 'pelvic' head out of the pelvis. I thought of trying to push back the baby which was already born up to its neck, but this seemed an impossible thing to do. A destructive operation on one baby was a very difficult decision to make, especially as the first baby was vigorous and its cord beating well. The anaesthetist was about 10 minutes away and I felt that to wait for him would have resulted in at least the loss of one of the babies. Being in a desperate position I adopted an unusual procedure.

The patient having previously been delivered naturally of a baby weighing over 9 lb., and her perineum being very lax, I felt that if forceps could be applied to the after-coming head of the breech baby it might be possible, under the protection of the forceps, to pull it past the head of the second baby. So the episiotomy which had been performed was widened considerably. The patient was told to breathe her trilene as hard as she could and she cooperated magnificently. The whole hand was introduced into the vagina and with a little difficulty forceps applied to the after-coming head. This necessitated introducing the forceps past the head which was in the pelvis, and this was not easy, but eventually the forceps were applied and locked easily. I then had a curious feeling that all would be well. Firm, steady traction was applied and in a little while the whole perineum was seen to gape enormously. I was prepared to deal with a 3rd-degree tear, which seemed to be the only real danger in this manoeuvre, but happily no such accident occurred. The next thing that one saw was a head being born; but it was not the head in the forceps—it belonged to the second baby. With the delivery of the second baby's head the head of the breech baby was easily born and the second baby followed soon after. The placenta was soon delivered and the episiotomy re-sutured. The mother's condition remained good.

The babies were both alive and weighed 3 lb. 9 oz. and 3 lb. 14 oz. at birth. The breech baby was slow in getting started but, aided by the paediatrician and excellent nursing sisters, both babies did well and a year later were stated to be thriving. I hope they are still.

*Discussion.* When we spoke about this rather fantastic delivery next day the point was raised whether it would not have been better to apply forceps to the second baby's head in the pelvis, which would have been easy, and not to the other head. I felt, possibly wrongly, that the shoulders of the second baby might catch on the first baby's head and become impacted.

What happened was that both heads came down together and the second baby's shoulders could engage because the after-coming head of the breech baby was pulled down into the pelvis by the forceps and was therefore out of the way—which it would not have been had forceps been applied to the head of the second baby in the pelvis. The manoeuvre could only be used with premature

babies and in this case it was because the mother had a big pelvis and lax tissues that the manipulations were possible. Obviously if there had been rigid tissues or a contracted pelvis the method would have been absurd. The result was fortunate; but because the same thing is likely to happen again I am recording the case so that, should any other doctor have a hair-raising experience of this nature, he may appreciate what is possible and may be able to adopt a similar procedure with greater assurance.

There is no doubt that this situation can occur again. It is strange that it should arise so rarely. Prematurity is almost the rule with twins and a breech followed by a vertex delivery is the third commonest position in which twins are born. Twins are commoner in multiparae and thus the stage is always set for a recurrence of this situation.

David Barron

Colonial Mutual Buildings,  
106, Adderley Street,  
Cape Town.

30 November 1955.

## SPECIALIST AND CONSULTANT REGISTER

To the Editor: I have a very great respect for my friends the specialists (whom I find high, wide and handsome—and affluent). Indispensable in modern medicine, exceedingly helpful and courteous to us general practitioners, most capable at their jobs; yet some, like *Junior Specialist*<sup>1,2</sup> and *Senior Specialist*,<sup>3</sup> are incapable of seeing further than their noses—or, possibly, pockets. Witness their paralogical arguments; for, in their angry panic at the growing public and professional dissatisfaction with prevailing practice, they both permit themselves to trail the good old red herring. How on earth does a consultant register prevent freedom of choice of doctor? It certainly will prevent wrong choice of specialist—patients seeking the ophthalmologist when the physician or dermatologist is more appropriate, or the urologist for his backache when the general practitioner is the better guide; or seeking specialist treatment for simple conditions as easily—if not better—treated by the family doctor; or expensive undertakings—such as a urological or gynaecological undertaking for a backache which turns out to be (and would have been diagnosed as such by the general practitioner) a simple fibrositis or a psychogenic condition; or squads of specialist practitioners treating various bits of one patient's anatomy for minor complaints (an ENT specialist for simple sore throat or wax in the ear, an ophthalmologist for accompanying conjunctivitis, a gynaecologist for pruritus vulvae, a surgeon for a simple skin fibroma) which can quite easily be treated by one doctor—the general practitioner.

*Senior Specialist* and *Junior Specialist* surely hold a low opinion of their colleagues by maintaining that a consultant register is going to drive specialist practitioners to dichotomy. Those specialists who seek to promote their practices by dichotomy will do so, consultant register or no consultant register.

The proof that specialists are in fact going beyond their scope lies in the proportion of specialists to general practitioners. It should be simple enough to check these proportions against accepted actuarial figures of how many of each speciality are required per number of general practitioners. Specialist work is essential, but batches of specialist practitioners doing the work of one general practitioner is not only expensive medicine but it is bad medicine.

A great deal of bad and expensive medicine is being practised precisely because of the peripatetic patients the specialist register encourages. Bogeys like 'no free choice of doctor' and 'dichotomy' are merely evasive tactics which project, I suspect, personal fears. Far too many specialists swallow patients referred to them—giving a course of vitamin injections and continuing investigations and simple therapies belonging properly to the general practitioner who referred the patient. Often they refer patients to someone else and not back to the doctor who sent the patient. The way in which patients are sent from specialist to specialist is a well-known scandal (a subtle form of dichotomy) and, if *Junior Specialist* and *Senior Specialist* are going to call in the public to adjudicate in the matter of the consultant register, they will hear of these and other scandals in no uncertain terms.

*Junior Specialist* fears he will lose his living under a consultant register, or have to revert to general practice. He will if he is redundant; and he is redundant only if under the guise of a specialist he is doing a general practitioner's job—at special rates. How could the specialists lose under a consultant register if the work they do is necessary? A consultant register is bound to promote (not demote) the practice of necessary and proper consultations by general practitioners with specialist practitioners, which is necessary in the present practice of medicine; and the patient would still have free choice of consultant, though he would be guided in choosing the right kind of consultant—a gynaecologist and not a urologist (or *vice versa*) and so on. But which particular gynaecologist, or urologist, or other specialist to go to would be his own free choice.

If medicine is to be whole and integrated all of it must begin (and much of it end) in the *general family doctor* and his relationship with the patient. Some specialists want jam on both sides of their bread—at the expense of the public. They want to be both family doctor (with its responsibilities, privileges and prestige) and specialist (with its privileges and prestige). Such ambivalence detracts from the true and proper and scientific practice of medicine.

After all, the specialists who are virtually consultants—radiologists, pathologists, anaesthetists—are neither inimical to free choice of doctor nor furthering dichotomy. Far greater abuses flourish under the specialist register than the few fairly harmless abuses it was intended to stop. Custom and tradition and moral education are stronger forces than legal enactments. But legal enactments in fact engender bad custom, as does the specialist register. Unguided free choice of specialist keeps some inferior specialists going, and they are the ones who are most fearful of the consultant register, for the opinion of a man's colleagues is a better guide to the patient in his choice of specialist than the advertisement which the specialist register provides for all and sundry. Unguided free choice of doctor sends a large proportion of patients seeking the wrong kind of specialist—and obtaining much and unnecessary investigation and treatment. I can quote case after case of patients who have spent hundreds of pounds—and ended up where they should have begun: in the general practitioner's hands. A rational free choice of specialist, which is something the public normally wants, has been woodooed from them by subtle and suggestive advertisement fostered by the specialist register.

There is nothing perfect in this world, every group must make allowances for imperfections. The shopkeepers allow a percentage for theft; each profession allows for abuse which cannot be controlled by law or police—only by moral persuasion.

The specialist register is a sledge hammer to kill flies. When you wield this instrument you may or may not kill a few flies; you certainly will break a lot of furniture—as witness the political temper of *Junior Specialist*: 'It is high time the specialists aroused themselves from their apathy and took active measures to ward off the danger that confronts . . .'. We have not seen a more dangerous statement for a long time, a sign of narrow outlook engendered and furthered by the specialist register which has served to divide the profession into general practitioners and specialists. The true and whole practice of medicine demands that all practitioners shall be doctors and colleagues, amongst whom a number are general practitioners and a few are specialists in particular fields. Each speciality tends to group together in the furtherance of its work, but that all specialist ranks are called upon politically to align themselves against the rest is indeed the wildest kind of dangerous medical politics. Fortunately those of us general practitioners and specialist practitioners who still maintain cordial relations, a proper sense of proportion and a sound and high professional tradition are not likely either to be stampeded by such madness or to sever our links of practice or friendship.

#### Senior General Practitioner

1. *Junior Specialist* (1955): S. Afr. Med. J., **29**, 1020.
2. *Idem* (1955): *Ibid.*, **29**, 1104.
3. *Senior Specialist* (1955): *Ibid.*, **29**, 1104.

#### MITRAL VALVOTOMY

**To the Editor:** We were interested to read the experiences of Dr. Schrire and his associates with their carefully studied small series

of patients subjected to mitral valvotomy.<sup>1</sup> Several points made by them call for comment:

1. While it is accepted that cases with irreversible congestive cardiac failure should be put in grade 4, we believe that many patients in grade 2 or 3 have a history of reversible congestive heart failure. The operative mortality in the latter cases is not strikingly higher than the average. We were surprised at the fact that 13 cases (17%) of the series were operated on while in congestive cardiac failure. In our experience of over 200 patients subjected to mitral valvotomy, only 6 (less than 3%) were in congestive failure at the time of operation, many others being brought out of failure by medical treatment prior to surgery.

2. The incidence of angina pectoris (23%) is considerably higher than that noted by other observers (Wood 12%,<sup>2</sup> Logan and Turner 2%). We wonder whether Dr. Schrire *et al.* are not labelling as angina pectoris what Logan and Turner call 'paradyspnoeic pain'.

3. There is a contradiction in that, while it is stated that 'in a small proportion of cases . . . a second obstruction develops in the pulmonary arterioles', it is later noted that 'severe pulmonary hypertension was present in 29%'. As some patients with moderate pulmonary hypertension have an increased pulmonary arterial resistance, the proportion of cases with a 'second obstruction' can hardly be called small.

4. We should be interested to know how the size of the cavity of the left ventricle was determined after valvotomy.

5. As the series contained only 5 patients with slight pre-operative mitral incompetence and as 2 of these obtained excellent results, the statement that 'the presence of incompetence even if slight considerably reduces the chances of success' is hardly justified. Nevertheless, as rigid calcified valves are commoner in patients with incompetence (Baker *et al.*)<sup>4</sup> and as full splits of such valves are often not possible, the results in patients with incompetence, even if slight, might be expected to be less impressive than in those patients with pure mitral stenosis.

6. In our experience of patients subjected to repeat valvotomies the cases consisted of those whose first operation was performed early in the surgeon's experience and in whom the valvotomy was probably inadequate, and one patient who had an attack of overt rheumatic fever 2 years after operation and at a second operation after another 2 years was found to have tight mitral stenosis. It is our impression that 're-stenosis' is probably less likely in patients who have had their valves widely split.

M. M. Zion  
B. A. Bradlow

701 Ingram's Corner  
Kotze and Twist Streets  
Johannesburg  
8 December 1955

1. Schrire, V., Vogelpoel, L., Phillips, W. and Nellen, H. (1955): S. Afr. Med. J., **29**, 1108 (26 November).
2. Wood, P. (1954): Brit. Med. J., **1**, 1052.
3. Logan, A. and Turner, R. (1952): Lancet, **2**, 1286.
4. Baker, C., Brock, R. and Campbell, M. (1955): Brit. Med. J., **2**, 983.

#### FUNCTIONAL AND PSYCHIC ELEMENTS IN HEART DISEASE

**To the Editor:** I wish to congratulate my friend Albert Rabinowitz on his concise article<sup>1</sup> under this title, which I read with great interest. I feel however that I must disagree with the view that X-ray and ECG examinations are necessary in cases in which clinically there is no cardiac enlargement, organic murmur, cardiac failure or angina pectoris. It is frequently the ECG examination which is causing functional heart disease, when a firm and authoritative 'It is not your heart at all, but your general nervousness' is the only correct therapy.

I should like to add that there are many people with pain in the left side of the chest who imagine they have some heart trouble. The pain is frequently due to rheumatic disease of the cervical or thoracic spine. This should not be overlooked.

Nathan Finn

27 C.N.A. Building  
East London  
9 December 1955

1. Rabinowitz, A. (1955): S. Afr. Med. J., **29**, 1129 (3 December).

Cape T.

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